Comparing the Reliability of Asthma Control Instruments: Clinic Questionnaire versus Daily Diary

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Objective: To determine if the Asthma Control Questionnaire is a more reliable measure of asthma control than the Asthma Control Diary among symptomatic asthma patients in Philippine General Hospital Out Patient Department.
Study design: Descriptive cross sectional
Study setting: Philippine General Hospital, Out Patient Department
Study population: Symptomatic asthma patients ages 18 and above who are on regular follow-up from August 2003 to January 2004
Maneuvers: Patients answered the diary at home for one week. Clinic questionnaire was administered by the clinician on clinic follow-up at the end of Week 1 and Week 2. The questionnaire and the diary were compared. The following measures were determined: proportion of stable patients, reliability and concordance.
Results: A total 35 patients were included in the study. Thirty two (91.4%) contributed to the stable group. Reliability tests utilizing the stable group showed that the within-sample variation for the questionnaire and diary were 0.14 and 0.18, respectively. These resulted in the questionnaire having better reliability (ICC = 0.82) than the diary (ICC = 0.65). The alpha reliability was also higher for the questionnaire (0.90) than the diary (0.79) indicating a stronger internal consistency between the mean of the items for the questionnaire than for the diary. The overall concordance or agreement between the Asthma Control Questionnaire and the Asthma Control Diary was high exhibiting an ICC of 0.83 for week 1 and ICC = 0.82 for week 2.
Conclusions: Both the Asthma Control Diary and the Asthma Control Questionnaire measure the same construct (asthma control) but the questionnaire has a stronger reliability than the diary. The overall concordance or agreement between the two- was high. If one weighs the practical advantages and disadvantages of a diary versus a questionnaire for measuring asthma control in clinical trials, the advantages of a questionnaire outweigh those of a diary. This is also true for monitoring patients in the general out-patient clinics where pulmonary function testing and peak flow monitoring are not routinely done. *Phil Journal of Chest Diseases. Vol 14 No. 1 pp: 1-5*

Keywords: Asthma questionnaire, Asthma control, Asthma diary

Introduction

Asthma continues to be a substantial cause of morbidity absence from work and use of health services among adults and children. In the Asia Pacific region alone, current levels of asthma control fall markedly short of goals specified in international guidelines for asthma management.[1] For many years the effectiveness of new asthma medications have been assessed by measuring the impact of clinical outcomes such as expiratory flow rates[2] symptoms, the need for other medications and airway hyperresponslvess.[3]

Various questionnaires have been proposed to assess asthma control. There are few methods available to globally quantify such control such as Mini Asthma Quality of Life Questionnaire[4] and Asthma Control Questionnaire (ACQ).[5] Recently a new method based on 0 to 100% scoring system has been proposed.[6] However in the measurement of functional status or quality of lifer a gold standard or criterion measure is not available.

Most asthma guidelines recommend assessing asthma control according to a series of criteria based on symptoms and pulmonary function. Education in asthma self-management, which involves self-monitoring by either peak flow or symptoms coupled with regular medical review and a written action plan improves health outcomes for adults with asthma. In one study peak flow monitoring was not superior to symptoms for adjusting the treatment according to an action plan.

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It has been often been assumed in the absence of formal evidence that more: accurate and precise data may be obtained if patients complete daily diaries than if they are asked to recall their experiences during a clinic visit.

The Asthma Control Questionnaire was developed and validated to measure asthma control in adults. It is completed in the clinics asks patients to recall their experiences during the previous week, and includes a measure of FEV_1 predicted. The Asthma Control Diary (ACD) has almost identical symptoms and medication to the questionnaire and has the same response options. In only one study published,[9] the ACQ has strong evaluative and discriminative properties and can be used with confidence to measure asthma control.

In general practice, assessment of asthma control is based primarily on symptoms and daily activities rather than objective assessment of airflow obstruction, such as spirometry or peak expiratory flow determination. In clinical trials, diary data are notoriously of poor quality. Reasons for this include lost diaries, forgotten entries, illegal and spoiled responses, and possible falsification.

In the PGH Out Patient Department, assessment of asthma control is done during the clinic visit based on symptoms recalled one or more weeks prior to the visit. No formal questionnaire is being used. Majority of patients cannot afford pulmonary function testing nor peak flow monitoring at home. This study is therefore aimed to utilize the ACQ and verify if it is a more reliable measure of asthma control than the daily diary, thereby challenging the assumption that the daily diary provides a superior estimate of clinical status among asthmatic patients.

Methodology

Study Design: Descriptive cross-sectional study design

Study Setting: Philippine General Hospital, Out Patient Department

Study Population: 1. Inclusion Criteria: Symptomatic asthma patients regardless of severity with ages 18 and above and on regular follow-up at PGH-OPD from August 2003-Jan 2004. All patients were using as needed inhaled bronchodilators.

2. Exclusion Criteria: a) Patients with significant pulmonary co-morbidities such as COPD, heart failure, cor pulmonale and chest wall abnormalities; b) Respiratory infections requiring antibiotics and/or hospitalization at enrollment or any time during the study; c) Inability to follow instructions.

Sample size calculation: To detect a correlation coefficient of at least 0.6 at 0.05 level of significance and 0.9 power, at least 32 subjects were needed.

Maneuvers Symptomatic asthma patients 18 years old and above who were on regular follow-up at Philippine General Hospital Out Patient Department were asked to sign an informed consent agreement at enrollment. Patients started answering the questions in the Asthma Control Diary on the day the consent was given. The diary was answered daily for seven consecutive days. They were followed up after one week (Week 1) and then 2 weeks (Week 2) from completion of the first diary. For one week before the second visit, patients completed the Asthma Control Questionnaire. The questionnaire was administered by the researcher clinician during each clinic visit Because of the foreseen financial constraints of the patients; spirometry and daily peak flow measurements were not included in monitoring asthma control. The study is limited to three weeks duration to minimize drop-outs and noncompliance among subjects.

The Tagalog version of the ACQ and ACD were lifted from the Asthma Quality of Life Questionnaire (AQLQ) Self Administered Filipino version as translated by MAPI Research Institute. The questionnaire is being used by the National Asthma Epidemiology Study (NAES), Validation study of the Tagalog version has been concluded in 2003 but final report is still not available.

Operational Definitions:

1. *Clinically stable group* - patients whose scores were the same or within 1 score below or above the baseline scores on the ACD during Week 1 and Week 2.

2. *Reliability* - refers to the reproducibility of a measurement, whether the test consistently yields more or less the same results when administered on several occasions on stable subjects.

3. Concordance - the agreement between the questionnaire and the diary.

4. *Responsiveness* - the likelihood of detecting a clinically important treatment effect, this measures the changes among subjects in the unstable group. This is sometimes referred to as the sensitivity of the test.

5. *Discriminative measurement* - instrument which measures differences between people, this is tested by measuring the reliability

6. *Evaluative measurement* - instrument which measures the change over time, this is tested by measuring responsiveness

Table I. Questionnaire and Diary Scores at the End of Week 1

	Questionnaire mean ± (SD)	Diary mean ± (SD)	Difference between Questionnaire and Diary (p value)
All questions	1.83 ± 0.96	1.59 ± 0.81	0.001
Symptoms alone	1.93 ± 1.01	1.66 ± 0.83	0.000
Nocturnal waking	1.91 ± 1.24	1.49 ± 0.82	0.006
Morning symptoms	1.31 ± 1.02	1.32 ± 0.90	0.003
Activity limitation	2.00 ± 1.28	1.76 ± 0.97	0.008
Short of breath	2.43 ± 0.98	1.91 ± 0.82	0.000
Wheeze	1.91 ± 1.42	1.82 ± 1.21	0.440
Inhaler use	1.37 +1- 1.09	1.23 +1- 0.95	0.210

Table II. Questionnaire and Diary Scores at the End of Week 2

	Questionnaire mean ± (SD)	Diary mean ± (SD)	Difference between Questionnaire and Diary (p value)
All questions	1.71 ± 0.83	1.45 ± 0.75	0.012
Symptoms alone	1.75 ± 0.86	1.50 ± 0.80	0.012
Nocturnal waking	1.68 ± 1.17	1.49 ± 0.93	0.107
Morning symptoms	1.50 ± 1.05	1.24 ± 0.88	0.066
Activity limitation	1.62 ± 1.13	1.51 ± 1.02	0.439
Short of breath	2.03 ± 0.97	1.71 ± 0.82	0.039
Wheeze	1.81 ± 1.09	1.57 ± 0.92	0.135
Inhaler use	1.50 ± 1.14	1.22 ± 0.80	0.047

Statistical Analysis One of the more important aspects of assessing the precision of instruments is reliability. Reliability refers to the reproducibility of a measurement which is quantified by simply taking several measurements on the same subjects. Poor reliability degrades the precision of a single measurement and reduces the ability to track changes in measurements in the clinic.

The most common form of reliability is retest reliability which refers to the reproducibility of values of a variable when the same set of subjects is measured twice or more. In this study reliability of the Asthma Control Diary and the Asthma Control Questionnaire was measured employing several statistical methods. One involved testing the difference between computed means of both asthma instruments across several categories using a paired *t-test*. Another is the use of retest correlation to measure reproducibility as well as the degree of association. A retest correlation is one way to quantify reliability: a correlation of 1.00 represents perfect agreement between tests whereas 0.00 represents no agreement whatsoever. When test and retest values are plotted, the closer the values are to a straight line, the higher the reliability. The correlation coefficients used in the study were the Pearson's correlation coefficient and the intra-class correlation coefficient (ICC). Computations were done using the Statistical Package for the Social Sciences (SPSS).

Testing the measurement properties of the questionnaire and the diary also required defining a group of patients who remained clinically stable between clinic visits (Week 1 to Week 2) and another group who experienced change in their asthma control. For the time period, each patient was categorized according to the clinician's global rating of change (stable group= scores of -1, 0, +1; unstable group = all other scores.) In this study, however, only three respondents could be classified under the unstable group. Hence, 32 out of the 35 patients contributed observations to the stable group. Reliability was estimated as the within-subject standard deviation and was related to the total standard deviation as an ICC.

As an added measure, the alpha reliability was also compared. The alpha reliability of the variable is derived by assuming that each item represents a retest of a single item. Although it is not a measure of test-retest reliability, the alpha reliability is a measure of internal consistency of the mean of the items at the time of administration of the questionnaire

Results and Discussion

There were a total of 53 respondents. Seventeen were lost to follow-up after the first clinic visit and were able to answer only the Asthma Control Diary and Asthma Control Questionnaire after Week 1. One subject was excluded for incomplete data. Only 35 respondents were finally entered into the study. Thirty two (91.4%) contributed to the stable group.

Although the wordings used for the symptom questions and response options were almost identical in the two instruments, absolute scores were consistently higher for the questionnaire than for the diary, consistent with the results of a previous study.[9] This is true for calculations done for both time periods: at the end of week 1 (*Table I*) and end of week 2 (*Table II*).

Except for morning symptoms in *Table I*, all other items in both Tables were, scored worse (higher) in the questionnaire. It could be speculated that when patients score the questionnaire, they may remember their worst experiences during the week. It may also be possible that patients tend to aggravate the state of their condition in the presence of medical personnel, perhaps to seek more

Table III. Concordance and Correlation between Questionnaire and Diary: Week 1

	Concordance between Questionnaire and Diary (ICC)	Correlation between Questionnaire and Diary (Pearson's r)
All questions	0.83	0.84
Symptoms alone	0.84	0.85
Nocturnal waking	0.65	0.69
Morning symptoms	0.72	0.74
Activity limitation	0.87	0.89
Short of breath	0.70	0.70
Wheeze	0.82	0.83
Inhaler use	0.74	0.75

Table IV. Concordance and Correlation between Questionnaire and Diary: Week 2

	Concordance between Questionnaire and Diary (ICC)	Correlation between Questionnaire and Diary (Pearson's r)
All questions	0.82	0.82
Symptoms alone	0.84	0.84
Nocturnal waking	0.76	0.79
Morning symptoms	0.76	0.77
Activity limitation	0.83	0.83
Short of breath	0.63	0.65
Wheeze	0.75	0.77
Inhaler use	0.73	0.77

medical attention. Then again, in the case of free medical services this would mean more than the necessary medical assistance in the form of medicines or treatment.

One limitation of the study was the fact that patients completed the daily diary before completing the questionnaire, and completing the diary may have influenced responses to the questionnaire. However, to compare the scores and the measurement properties of the two instruments, it was necessary for patients to be in exactly the same clinical state and to record their experiences over the same time period when completing the two instruments. Another limitation was that falsification of diary entries cannot be checked.

Findings show that except for "wheezing" and "inhaler use" there was significant differences in scores between all items in the diary and questionnaire. This suggests that recall did not seriously influence the results of the study at the end of week 1. By week 2, however, differences between the means were not as pronounced particularly for the item "activity limitation" suggesting that recall bias· may have influenced the results.

Further examination of *Tables I* and *II* also shows that consistently higher standard deviation scores were registered for the questionnaires indicating a wider spread of values than those obtained for the diary. This may be because of smaller deviations within subjects because of the tendency to repeat scores on a day to day basis, as in the case of the diary. Again, this finding is true for both time periods.

Nevertheless, correlations between the Asthma Control Questionnaire and the Asthma Control Diary were significant (*Tables III* and *IV*). The Pearson correlation coefficients between the two instruments for overall score symptoms were high. Only the correlations for "nocturnal waking," and "shortness of breath" were moderate for week 1 and week 2, respectively. This shows a high reproducibility of the rank order of subjects on retest. It indicates that the subjects will mostly keep their same places between tests.

The usual Pearson correlation coefficient, however, usually overestimates the true correlation for small sample sizes. A better measure of the retest correlation is the intra-class correlation coefficient or ICC. It does not have this bias with small samples, and it also has the advantage that it can be calculated as a single correlation when there are more than two tests. In fact, ICC is equivalent to the appropriate average of the Pearson correlations between all pairs of tests.

In this study, overall concordance or agreement between the Asthma Control Questionnaire and the Asthma Control Diary was high exhibiting an ICC of 0.83 for week 1 and ICC of 0.82 for week 2. Following the pattern of the Pearson's correlations, concordance were also high for all other items except for "nocturnal waking" for week 1 and "shortness of breath" for week 2. At the outset, if one only considers the high concordance or agreement between the two instruments it may be safe to say that one can either use the diary or the questionnaire. Nevertheless, computed means for the questionnaires were consistently higher and significantly different than those of the diary, which goes to show that one cannot be used interchangeably with the other. Either one uses the diary consistently or the questionnaire alone.

Consistent with a previous study, reliability tests utilizing the stable group show that reliability tended to be better for the questionnaire than for the diary. This suggests that the two instruments measure the same construct (asthma control) but that the questionnaire has stronger reliability than does the diary. The within-sample variation for the questionnaire and diary were 0.14 and 0.18, respectively. These resulted in the questionnaire having better reliability (ICC=0.82) than

the diary (ICC=0.65). The alpha reliability was also higher for the questionnaire (0.90) than the diary (0.79) indicating a stronger internal consistency between the mean of the items for the questionnaire than for the diary.

Because only three (8.6%) patients were in the unstable group, responsiveness could not be measured and evaluative testing could not be done.

Conclusion

Of the 35 subjects, 32 (91.4%) were in the stable group. Reliability tests utilizing the stable group showed that reliability tended to be better for the questionnaire (ICC = 0.82) than for the diary (ICC = 0.65). The alpha reliability was, also higher for the questionnaire (0.90) than the diary (0.79) indicating a stronger internal consistency between the mean of the items for the questionnaire than for the diary. These are consistent with a previous study[9] wherein the Asthma Control Questionnaire had a better discriminative property than the diary.

The overall concordance or agreement between the Asthma Control Questionnaire and the Asthma Control Diary was high exhibiting an ICC of 0.83 for week 1 and ICC = 0.82 for week 2, Following the pattern of the Pearson's correlations, concordance were also high for all other items except for "nocturnal waking" for week 1 and "shortness of breath" for week 2.

The ultimate question is whether one should use a questionnaire or a diary. If one weighs the practical advantages and disadvantages of a diary versus a questionnaire for measuring asthma control in clinical trials, the advantages of a questionnaire outweigh those of a diary. This is also true for monitoring patients in the general out-patient clinics where pulmonary function testing and peak flow monitoring are not routinely done.,

Recommendation

The Asthma Control Questionnaire can be used in the out-patient clinics for monitoring asthma control, however, it is still recommended that objective measures such as spirometry or peak flow monitoring coupled with symptomatology is done to strengthen the results of the study.

Further tests are also required before one can consider relinquishing the use of diaries in asthma clinic trials in favor of the Asthma Control Questionnaire. Tests on validity still need to be done. This entails accomplishing other sets of questionnaires to validate the computed values as well as comparing obtained results from findings of previous studies. It is generally accepted that once reliability and validity have been established, the test is ready for use as an outcome measure in clinical trials.[10]

Moreover, the study may have to be extended for more than a three-week period to be able to capture an adequate sample for measuring unstable patients. This would enable the researcher to assess the instruments for responsiveness in detecting changes in the patients whose asthma was unstable and to differentiate these patients from those whose asthma was stable.

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The Association between Objective Findings and Subjective Symptoms of Asthmatic Adults Seen at VMMC

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Background Asthma care involves a spectrum that starts from its diagnosis to its management, control, and prevention of attacks. Though the guideline dictates this to be so, its delivery to the patients may differ. Oftentimes, treatment is based solely or the subjective symptoms experienced by the patient. This practice is misleading and erroneous as integration of both the subjective and objective findings of asthma are essential in the provision of care. The years saw an evolution of studies which seek to determine an association between these. However, it has remained elusive.

Objectives To determine the association between objective findings and subjective symptoms in adult asthmatic patients.

Methods This was a prospective cross-sectional study done for one year at Veterans Memorial Medical Center-OPD Clinic. Included were 27 patients that comprised males and females aged 18-80 years old, with persistent asthma for at least six months and upon spirometry with an FEV_1 %predicted (pre-bronchodilator) of 60-80%. Excluded were those with respiratory infections a month prior to inclusion, uncontrolled co-morbid medical illnesses, smoking history of > 10 pack years, pregnant and with use of medications for asthma other than short-acting inhaled beta-2 agonist. Subjects did spirometry and completed the Asthma Control Questionnaire on two subsequent visits done 12 weeks apart.

Statistical Analysis of Data The Spearman Rank Correlation of Coefficients was used for the analysis of the correlation between the subjective symptoms and the objective findings of asthma. The paired t-test was used for the analysis of measured FEV_1 % predicted at different observation periods (Visit 1 and 2). The Wilcoxon Matched-pairs Signed Ranks Test was used for the analysis of subjective symptom scores at different observation periods (Visit 1 and. 2).

Conclusion There is no association between the objective finding (FEV_1) and the total/symptom score. Nor was there an association between the objective finding and the individual subjective symptom. A comparison of the objective finding (FEV_1) on the two visits revealed a significant change. The degree of airway obstruction was improved after 12 weeks. Likewise, the subjective symptom score was also improved during this time. *Phil Journal of Chest Diseases. Vol. 14 No. 1 pp: 6-10*

Keywords: Asthma symptoms, Asthma severity, Asthma control

Introduction

Asthma care commences from the time of diagnosis to the whole spectrum of management, control, and prevention of subsequent attacks. It requires an evaluation of both the subjective symptoms experienced and the objective findings of pulmonary status manifested by the patient involved.

Though, this may be the guideline, delivery of asthma care may differ. Oftentimes, asthma is diagnosed and managed solely on the basis of the degree of severity of subjective symptoms experienced.[1] This rampant practice, however, is misleading.

Whereby symptoms may improve, the objective findings may not. Asthma as perceived subjectively may differ from the asthma that is objectively measured.

This is not to say, however, that one is superior over the other as a measure of severity and control. Both are essential in asthma care. This is an aspect in asthma care that this study aims to explore - to determine if a congruency exists between the two measures in the assessment and improvement of asthma over a period of time.

With this study in our institution, the researchers may be able to present a picture of the disease using local subjects. A correlation derived from these two measures will help guide physicians in the treatment and control of the disease.

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Table I. Patient Characteristics (n=27)

Characteristic	Mean ± SD
Age, yr	37 ± 8.64
Duration of asthma %,(2:1-s5years)	22%
Gender, % female	77.8%
Smoking, % Current Past Never	 7% 11.1% 81.5%
FEV_1 L (% predicted) Pre-bronchodilator Post-bronchodilator	 66.997 ± 6.528 74.955 ± 7.824

Table II. Symptom Scores at Initial and Follow-up Visit

Symptom	Initial (Visit 1)	Follow-up (Visit 2)	Mean Difference	P value
Nocturnal awakenings	2.519 ± 1.014	0.222 ± 0.424	2.297	0.0000
Asthma symptoms upon waking up in the morning	2.222 ± 0.698	0.222 ± 0.424	2.000	0.0000
Activity limitation	2.333 ± 1.038	0.259 ± 0.594	2.074	0.0000
Shortness of breath	2.370 ± 1.006	0.296 ± 0.609	2.074	0.0000
Wheeze	2.000 ± 1.109	0.259 ± 0.526	1.741	0.0000

Methods

This was a prospective cross-sectional study done for a period of one year at Veterans Memorial Medical Center OPD Clinic.

A total number of 64 subjects providing for a 20% probability of subjects withdrawal, elimination and inability· to complete the· study were targeted. However, only 27 subjects who fulfilled the inclusion and exclusion criteria were selected.

The patients comprised of males and females aged 18-80 years old, with history of persistent asthma for at least six months. Upon spirometry, FEV_1 % predicted. (pre-bronchodilator therapy) was 60% to 80% predicted. Excluded from the study were those with history of respiratory infections a month prior to inclusion, uncontrolled co-morbid medical illnesses, positive smoking history of 10 pack years, pregnant and with use of medications for asthma other than short-acting inhaled beta-2 agonist.

On the first visit, complete history and physical examination of the subjects were done. Thereafter, patients were subjected to spirometry (pre- and post-bronchodilator) testing.

The Asthma Control Questionnaire (ACQ) was also answered. The subjects were asked to answer the first six questions of the ACQ. It consisted of respiratory symptoms (nocturnal awakenings, asthma symptoms on waking in the morning, activity limitation, shortness of breath, wheeze) and use of short-acting bronchodilator over the previous week. The severity of symptoms was scored accordingly from 0 (which pertained to no impairment or limitation) to 6 (total impairment or limitation).

The last item was filled, by the researcher. The subject's FEV_1 as percentage of the predicted normal was scored accordingly from 0 (which pertained to > 95% predicted) to 6 which corresponded to < 50% predicted).

Subjects were prescribed a fixed dose combination of steroid and long-acting beta-2 agonist. Instructions on the proper use of the medication and the importance of medical compliance were conveyed. Subjects were instructed to come back for a follow-up visit after 12 weeks (Visit 2).

On the second visit, subjects again underwent the same procedures (history-taking and physical examination, spirometry, and completion of Asthma Control Questionnaire or ACQ).

Statistical Analysis of Data: The Spearman Rank Correlation of Coefficients was used for the analysis of the correlation between the subjective symptoms and the objective findings of asthma. The paired t-test was used to compare measured FEV_1 % predicted at different observation periods (Visit 1 and 2).

The Wilcoxon Matched-pairs Signed Ranks Test was used to compare subjective symptom scores at different observation periods (Visit 1 and 2).

Results

A total of 27 patients were included in the study (*Table I*). It comprised 6 males (22.2%) and 21 females (77.7%). Majority of the population was in the 31-40 year old age bracket with a mean age of 37 years old. Most were nonsmokers (81.5%), and with asthma duration of 1-5 years (22%). Co-morbid conditions identified among the subjects included diabetes mellitus, hypertension, and nodular non-toxic goiter; all of which were adequately controlled with medications.

With five symptoms in the ACQ graded accordingly from 0 to 6, a total ranging from 0 to 30 is possible. The relationship between the degree of airway obstruction, as

determined by the FEV_1 and the total asthma symptom score was evaluated.

Statistical analysis revealed no relationship between these two parameters. ($r = 0.1092$, $p = 0.588$) on the initial visit. On the subsequent visit (Visit 2), still no relationship existed between these two parameters ($r = 0.0152$, $p = 0.940$).

On testing the relationship between any of the individual subjective symptoms and objective finding of asthma, still no relationship existed between these two. In the comparison of the FEV_1 % predicted between Visit 1 and 2, using the paired t-test, a significant change and improvement was noted with a computed mean difference of 7.9578 and a p value of 0.000.

In the analysis of the individual symptom scores on two subsequent visits, a significant improvement in symptoms experienced was noted on comparison of the values using the Wilcoxon Matched-Pairs, Signed-Ranks Test with a noted p value of 0.000 for each individual asthma symptom. (*Table II*).

Discussion

In the present study, analysis of data revealed a significant improvement in asthma symptom score in the two subsequent visits. This is also true with the analysis done on data accumulated on FEV_1 % predicted as tested in the two visits.

However, testing of these two parameters against each other to determine whether a relationship exist between the subjective symptoms and objective finding of asthma revealed none. The conclusion of this study done with local subjects seen at Veterans Memorial Medical Center is in congruency with existing studies that arrived at the same conclusions.

Patients with asthma frequently have poor recognition of their symptoms and poor perception of the severity - especially if their asthma is severe and longstanding. Assessments of symptoms by physicians may be inaccurate. Measurements of lung function, particularly in the reversibility of lung function abnormalities, provide a direct assessment of airflow Iimitation.[4]

In a study conducted by Teeter et al., chronically asthmatic .adult patients were included in a cohort study which determined the relationship between airway obstruction and respiratory symptoms[6] (i.e. cough, dyspnea, wheeze, chest tightness, sputum production, and nocturnal awakening). Respiratory symptoms were rated by patients on a 0 to 4 scale at initial and first follow-up clinical evaluations. Spirometry and PEF were measured at the initial clinic visit and PEF was measured at all follow-ups.

The results of the study showed that asthma symptoms did not correlate with the degree of airway obstruction as determined by the FEV_1 or percent predicted PEF vs. total symptoms. Subjective wheezing was the best individual predictor of the level of airway obstruction in this group of patients. When reassessed an average of 7.9 weeks later, patients reported significant improvement in several symptoms, including those of wheeze, chest tightness, dyspnea, and nocturnal awakening. However, this symptomatic improvement was not associated with improvement, in the level of airway obstruction.

The researchers came to the conclusion that asthma symptoms correlate poorly with the level of airway obstruction as determined by the FEV_1 and PEF. Following treatment, subjective improvement in asthma symptoms may occur without improvement in the level of airway obstruction.

These results support the recommendation to measure airway obstruction objectively when assessing adult patients with chronic asthma. In a study done by Sly et al among asthmatic children, no significant relationship exist between subjective symptom scores and FEV_1, both before and after a four-week "training period" during which peak expiratory flow was measured thrice daily.[8] Kendrick et al also arrived at the same conclusions with a study conducted among adult asthmatic patients. In this study, about 60% of 225 were poor discriminators of their underlying airway obstruction as determined by serial PEF over a two-week period.[7]

In addition to these studies, many asthmatics have been demonstrated to poorly perceive added airway resistance or airway obstruction induced. by inhaled pharmacologic agents . In effect, all these pointed to the lack of sensitivity of asthma symptoms for identifying the presence of underlying airway obstruction.[11]

This is essential as the weight that most physicians give on the symptoms experienced by asthmatic patients is significant. Most physicians base their treatment on the severity of the symptoms reported, and oftentimes, fail to test objectively and evaluate the degree of airway obstruction as reported by spirometry which is the standard that we follow in the objective evaluation of asthma severity.

The impact of this practice on the patient and the quality of life that he leads cannot be belittled. Suppose that a patient is an "under estimator" of symptom severity with an FEV_1 that points to a moderate to severe

asthma, and yet being treated with a level of care that is good only for an asthma classified as mild in severity. The costs (may it be financial, emotional, social and physical) may be too overwhelming for the patient. The restrictions placed on him by the disease, may just be too vast. Fatality even is a possibility that can never be far from mind. With this in mind, it is therefore of major importance that asthma care should be able to cover both.

As much as possible, patients should be treated with a level of therapy commensurate with their degree of airway obstruction for the following reasons: (1) the airway obstruction that occurs in asthma is thought to be a manifestation of airway inflammation; (2) airway wall remodeling and fixed airway obstruction are potential complications of chronic airway inflammation, which can be seen even in patients with clinically mild disease; and (3) a number of other well-known chronic diseases in asymptomatic patients, such as hypertension, hypercholesterolemia, and hyperglycemia are known to result in irreversible end-organ damage if left untreated.[11]

Therefore, treatment plan of asthma in terms of its long-term progress and treatment response should be able to incorporate both symptom severity and airflow limitation as parameters to better individualize it according to patient need. This study reiterates all of these with its findings on the association of objective symptom and subjective findings of asthma.

Conclusion

There is no association between the objective findings and subjective symptoms of asthma. On comparison of the spirometry results done on subsequent visits FEV_1 which is the objective finding of asthma used was improved significantly.

Symptom severity as based on the symptom score completed was also improved on comparison with the subsequent visits.

Limitations

In the completion of the study, the following were identified as limitations: a) *Sample Size* In the initial protocol, a total of 64 subjects; were proposed for inclusion to provide for a 20% probability of withdrawal, elimination and inability to complete the study. Only 27 subjects completed the study. Were a bigger population recruited to participate in the study, the results perhaps would have been different and a significant relationship between the subjective findings and objective finding may have been derived; b) *Study Duration* With a duration of 12 weeks in between the two subsequent visits, recruitment and inclusion of potential subjects to the study was hampered as potential ones seen in the latter part were· predicted not to complete it up to the second visit. These subjects therefore are lost. With a longer duration, more subjects may be included to participate and a bigger sample size may be achieved; and c) *Scoring system of the Asthma Control Questionnaire* Subjects answered a seven-point questionnaire that scored the symptom severity. A few found this to be too cumbersome and confusing as the difference in between the scores were perceived to be vague.

The authors tried to bridge this gap by facilitating and aiding the subjects while answering said questionnaire.

Recommendations

A longer study duration to enable the researcher to recruit a bigger sample size may render the research with more varied results. It will provide us with more solid conclusions as to the relationship that exists between subjective symptoms and objective finding of asthma. Other Asthma questionnaires are also available. These maybe used in lieu of the Asthma Control Questionnaire to assess the severity of symptoms experienced by the asthmatic patient.

An example is the Asthma Control Diary whose wording and response options are almost identical to that used in the Asthma Control Questionnaire. The only major difference is that peak expiratory flow rate (PEFR) is recorded instead of the FEV_1. The diary is scored by adding the responses for each of the Seven questions for each of the 7days, with resultant scores between 0 = good control and 6 = poor control

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Hospital-Based Physician Assessment of Knowledge, Attitudes and Practice in the Diagnosis and Management of Asthma Guidelines

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Objective*:* To determine the knowledge, attitudes and practice of hospital–based physicians belonging to different specialties and level of training in the diagnosis management and prevention of asthma, as stated in the Global Initiative for Asthma Guidelines 2002.

Materials and Methods*:* The study was conducted in a tertiary government hospital involving residents and consultants of Family Medicine, Internal Medicine, Pediatrics, Pulmonary Medicine practitioners and fellows in training. A 31-point questionnaire was distributed among the physicians concerned, consisting of eight core subject areas: assessment, asthma diagnosis, education, pathology, prevention pharmacology, severity and therapy. The score for each of the core subjects and the total score were calculated and were grouped according to the level of training of the physicians and their respective specialties. The calculated mean scores for each group of physicians were compared using one-way analysis of variance, with level of significance set at $p < 0.05$ and 95% confidence interval.

Results*:* A total of 144 (75.8%) physicians responded and returned the completed test questions out of 190 sent out. The mean score of the respondents was 45.8 $\pm$ 13.4% (mean $\pm$ SEM) performing best in questions pertaining to asthma diagnosis and scored poorly in prevention of asthma triggers. The pulmonary fellows in training got the highest mean of 59.7, SEM 12.3% compared to their respective counterpart as far as the level of training is concerned. The performance of the respondents in proper classification of asthma staging was 45.8 $\pm$ 13.4%. The medical interns got the lowest score at 40.6, SEM 10.3%. Among the eight subjects, the surveyed physicians performed least in asthma assessment, education, prevention, severity classification and therapy. Significant differences were noted in the understanding of the guidelines in subject areas concerning: asthma diagnosis ($p = 0.001$), pathology ($p < 0.001$), pharmacology ($p < 0.001$), severity ($p < 0.001$) and therapy; ($p < 0.001$). Across the different specialties, the pulmonary specialists got the highest mean score with 61.7, SEM 11.6% followed by the medical internists. Significant differences in their understanding of the guidelines were observed in question pertaining to asthma diagnosis ($p < 0.001$), assessment ($p = 0.026$), pathology ($p < 0.001$) pharmacology ($p < 0.001$), prevention ($p < 0.001$) and therapy ($p < 0.001$).

Conclusion*:* The study showed that there is a need for further improvement in the knowledge and understanding of the NHLBI Global Initiative for Asthma Report among the physicians in VMMC. Particular subject areas that should be emphasized in asthma guidelines dissemination among health care providers are proper assessment, importance of asthma education to patients, identification and prevention of asthma triggers, proper severity classification and choice of appropriate therapy. Continuing medical education through lectures, workshops, case interactive conferences and organization of asthma management program may be strategies to address these deficiencies and differences in the knowledge and use of guidelines. *Phil Journal of Chest Diseases. Vol. 14 No. 1 pp 11-16*

Keywords: Asthma guidelines, diagnosis, treatment

Introduction

Asthma is one of the most common chronic diseases worldwide, imposing, substantial social burden on both children and adults.[1] The growing burden of asthma greatly affects the productive age of the world population. To date, approximately 15 to 17 million persons are afflicted with the disease in the United States alone.[2] To address the burden of the disease, the National Heart, Lung and Blood Institute (NHLBI) developed the Guidelines for the Diagnosis and Management of Asthma in 1991. This report focused on the role of patient education and use of objective measures of lung function, including home peak flow monitoring. It recognized the role of inflammation in the pathogenesis of asthma and recommended anti-inflammatory medications for patients with moderate and severe asthma.[3] The guidelines were disseminated to physician: worldwide and translated into many languages. Revisions took place in 1997 and the NHLBI updated their recommendations in the Expert Panel Report 2 Guidelines for the Diagnosis and Management

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of Asthma (EPR-2). Through extensive research in the pathogenesis of asthma, this guideline further emphasizes the role of inflammation in its pathophysiology. Hence, anti-inflammatory medications found its role as mainstay of treatment. Further, the classification of the asthma severity was stratified as mild intermittent, mild persistent, moderate persistent or severe persistent. Three years after new scientific findings in the area of genetics, risk factors, natural history and pathogenesis of asthma, the Global Initiative for Asthma Executive Committee released the revised 2002 report. Based on this report, the operational definition of asthma appreciates the key role of the underlying inflammatory response in asthma.[4]

Despite the growing interest in guidelines formulation in the diagnosis and management of asthma, practice variation still persists among physicians who are resistant to follow and accept evidence-based guidelines. The lack of adherence to published guidelines appears to occur not only with patients living in poverty but also with those who are managed in certain health maintenance organizations.[3,5,6] In addition to these, the poor adherence to guidelines can be traced back to the lack of knowledge and understanding of physicians involved in the care of asthmatic patients.

In a study by Doerschug et al,[3] which assessed the practice of physicians with regard to asthma guidelines, the mean correct total score out of the 31 survey questions was 60%. Asthma specialists scored higher in pharmacology and prevention. However none of the surveyed physicians performed well on estimating disease severity. There were also deficits in the use of spirometry and anti-inflammatory agents. Hence such findings were of concern because there were some discrepancies in the physician understanding all (practice of the guidelines.[4] In contrast, a survey among primary care physician pertaining to the asthma care practices in a highly populated, urbanized and reported that almost half of the respondents utilized spirometry as part of their initial evaluation among newly diagnosed asthmatic patients. Identification and management of disease severity was estimated at 47.7% of the surveyed population.[5] Likewise, among pediatric asthmatic patients, family physicians and pediatricians varied in their practice as far as diagnosis is concerned. The former more likely utilized spirometry in diagnosis but were less likely to recommend daily peak flow measurements compared with the latter.[6] A survey was also conducted among emergency physicians assessing their concordance to asthma practice guidelines. Result showed that more than 60% of the 416 respondents administered beta-agonists and corticosteroids, in concordance with the recommendations. Forty-seven percent of the respondents reported measuring pre-treatment pulmonary function and only 38% reported checking pulmonary function prior to disposition.[7]

In the Philippines, the Philippine College of Chest Physicians Council on Asthma took the initiative of coming up with similar guidelines adapted from the 1994 Global Initiative on Asthma. This was the Philippine Consensus Report on Asthma Diagnosis and Management published and disseminated in 1996.[8]

In one local study[9] on asthma knowledge and understanding of training physicians in a tertiary hospital, the investigators cited the need for further dissemination of the guidelines, particularly in areas concerning asthma prevention and identification of triggers. Recommendations were laid down in ensuring continuous support in medical education through medical fora, lecture series and conferences among health care providers. Similarly, a retrospective study[10] or physician adherence to the Philippine College of Physician Consensus Report or Asthma showed that adherence is fair. Identification of signs and symptoms, severity classification and management prescription, however, needs improvement of adherence to the guidelines.

Indeed much effort had been initiated in asthma education and guideline dissemination. Presumably with the existence of such guidelines, more asthmatic cases should have been identified and managed accordingly, depending on the level of the chronic severity of the symptoms. However such is not the case and the reasons identified were non-adherence of physicians and their lack of knowledge and understanding to clinical practice guidelines.

In this study, we determined the awareness of the hospital-based physicians on the asthma guidelines and to assess their knowledge and understanding using a validated questionnaire containing the following subject areas: assessment, asthma diagnosis, education, pathology, prevention pharmacology, severity and therapy.

Materials and Methods

This is a cross- sectional study conducted in January 2004 at the Veterans Memorial Medical Center, a tertiary government hospital involving residents and consultants of family medicine, internal medicine, pediatrics, pulmonary medicine and fellows and medical interns. The estimated sample size, based on a 60% response was 256.

Table I. Results of asthma questionnaire by level of training

Level of Training	Mean scores SD (%, SEM)								
	Assessment (3 questions)	Diagnosis (3 questions)	Education (1 question)	Pathology (3 questions)	Pharmacology (6 questions)	Prevention (2 questions)	Severity (6 questions)	Therapy (7 questions)	Total no. of questions 31
Consultants (n=19)	1.68 ± 0.82 (56 ± 27)	2.21 ± 0.85 (73.6 ± 28)	0.21 ± 0.42 (21 ± 42)	2.16 ± 0.83 (72 ± 27.6)	3.42 ± 1.22 (57 ± 203)	0.68 ± 0.75 (34 ± 37.5)	3.58 ± 1.22 (59.67 ± 20.3)	4.20 ± 1.66 (0.8 ± 23.7)	18.21 ± 4.74 (58.7 ± 15.3)
Fellows (n=8)	1.63 ± 0.92 (54.3 ± 31)	2.63 ± 0.52 (87.7 ± 17.3)	0.38 ± 0.52 (38 ± 52)	2.38 + 1- 0.92 (79.3 ± 31)	3.75 ± 1.16 (62.5 ± 19.3)	0.63 ± 0.74 (31.5 ± 37)	3.50 ± 1.41 (58.3 ± 23.5)	3.63 ± 0.92 (51.8 ± 13.1)	18.50 ± 3.82 (59.7 ± 12.3)
Residents (n=37)	1.30 ± 0.74 (43.3 ± 24.7)	2.118 ± 0.89 (69.3 ± 29.7)	0.41 + 10.50 (41 ± 50)	1.43 ± 0.90 (47.7 ± 30)	3.43 + 1.26 (57.2 ± 21)	0.78 ± 0.58 (39 ± 29)	2.59 ± 1.14 (43.2 ± 19)	2.70 ± 1.22 (38.6 ± 17.4)	14.73 ± 3.66 (47.5 ± 11.8)
Interns (n=80)	1.30 ± 0.79 (43.3 ± 26.3)	1.69 ± 0.80 (56.3 ± 26.3)	0.36 ± 0.48 (36 ± 48)	1.34 ± 0.94 (44.67 ± 31)	2.56 ± 1.16 (42.67 ± 19.3)	0.47 ± 0.57 (23.5 ± 28.5)	2.40 ± 1.11 (40 ± 18.5)	2.33 ± 1.21 (33.3 ± 17.3)	12.59 ± 3.20 (40.6 ± 10.3)
Total (n=144)	1.37 ± 0.79 (45.7 ± 2.6)	1.91 ± 0.86 (63.7 ± 2.7)	0.35 ± 41.48 (35 ± 48)	1.53 ± 41.97 (51 ± 32.3)	2.97 ± 1.26 (49.5 ± 21)	0.59 ± 0.62 (29.5 ± 31)	2.67 ± 1.22 (44.5 ± 20.3)	2.75 ± 1.42 (39.3 ± 20.2)	14.21 ± 4.16 (45.8 ± 13.4)

Table II. Mean scores of asthma questionnaire according to different training specialties

Training Specialties	Mean scores SD (%, SEM)								
	Assessment (3 questions)	Diagnosis (3 questions)	Education (1 question)	Pathology (3 questions)	Pharmacology (6 questions)	Prevention (2 questions)	Severity (6 questions)	Therapy (7 questions)	Total no. of questions 31
Pulmonary Medicine (n=15)	1.60 ± 0.83 (53.3 ± 27.7)	2.60 ± O.51 (86.7 ± 17)	0.40 ± 0.51 (40.0 ± 51)	2.33 ± 0.82 (77.7 ± 27.3)	3.93 ± 0.96 (65.5 ± 16)	0.53 ± 0.64 (26.5 ± 32)	3.20 ± 1.26 (53.3 ± 21)	4.53 ± 1.51 (64.7 ± 21.6)	19.13±13.6 (61.7 ± 11.6)
Family Medicine (n=15)	1.47 ± 0.74 (49 ± 24.7)	1.60 ± 0.83 (53.3 ± 27.7)	0.20 ± 0.41 (20 ± 41)	2.20 ± 0.41 (73.3 ± 13.7)	2.67 ± 1.45 (44.5 ± 24.2)	0.33 ± 0.98 (16·5 ± 24.5)	2.67 ± 0.98 (44.5 ± 163)	2.27 ± 0.80 (32.4 ± 11.4)	13.40 ± 2.4 (43.2 ± 7.8)
Internal Medicine (n=28)	1.57 ± 0.74 (52.3 ± 24.7)	2.29 ± 0.90 (76.3 ± 30.0)	0.43 ± 0.50 (43 ± 50)	1.50 ± 0.96 (50.0 ± 32)	3.82 ± 1.02 (63.7 ± 17)	1.04 ± 0.64 (52 ± 32)	3.07 ± 1.39 (51.2 ± 23.2)	3.14 ± 1.43 (44.8 ± 20.4)	16.8(,±/4.69 (54.4 ± 15.2)
Pediatric (n=6)	0.50 ± 0.55 (16.7 ± 18.3)	2.17 ± 0.75 (72.3 ± 25)	0.17 ± 0.41 (17 ± 41)	0.50 ± 0.55 (16.7 ± 18.3)	2.67 ± 0.82 (44.5 ± 13.7)	0.83 ± 0.41 (41.5 ± 20.5)	3.00 ± 1.55 (50 ± 25.8)	3.33 ± 1.03 (47.(, ± 14.7)	13.17 ± 1.83 (42.5 ± 5.9)
Medical Interns (n=80)	1.30 ± 0.79 (43.3 ± 26.3)	1.69 ± 0.80 (56.3 ± 26.7)	0.36 ± 0.48 (36 ± 48)	1.34 ± 0.94 (44.7 ± 313)	2.5(, ± 1.16 (42.7 ± 19.3)	0.47 ± 0.57 (23.5 ± 28.5)	2.40 ± 1.11 (40 ± 18.5)	2.33 ± 1.21 (33.3 ± 17.3)	12.59 ± 3.20 (40.6 ± 10.3)

A 31-point self-administered validated questionnaire formulated by Doerschug et al[3] was distributed among the physicians concerned. The questionnaire consists of a multiple-choice test questions with single correct answer which addressed the following eight subject areas of concerns namely assessment, asthma diagnosis, education, pathology, prevention, pharmacology severity and therapy.

The questionnaire was distributed personally among the different training specialties in the hospital. A total of 190 physicians participated in the survey broken down into the following; Family Medicine staff (n=16) and residents (n=14), Pulmonary Medicine staff (n=12) and fellows (n=8), Internal Medicine specialists (n=19) and residents (n=32), Pediatric specialists (n=4) and resident: (n=5) and medical interns (n=80). To ensure high response rate to the survey clinic visits and telephone calls were the means for follow-up.

The completed questionnaire was manually checked to ensure that each number had a single correct answer. A total score and the score for each of the eight subject areas of concern were calculated for each participant. The scores were grouped according to the level of training of the physicians and their respective specialties. Data analyses were done using the SPSS software.

Mean scores for each subgroup were reported and compared using one way analysis of variance and Kruskal Wallis test, with level of significance set at $p < 0.05$, or 95% confidence level.

Results

A total of 190 physicians at different levels of training and specialties were surveyed, 144 (75.8%) of these responded· and returned the completed questionnaire. Out of the 144 respondents, 120 (83%) of them were aware that the guidelines exist and they were able to read and understand the contents. The breakdown of the respondents were as follows: pulmonary fellows-in-training (n=8, 100%), Pulmonary Medicine staff (n=7, 58.3%), Internal Medicine staff (n=5, 26.3%) and

residents (n=23, 72%), Family Medicine practitioners (n=5, 31%) and residents (n=10, 71%), pediatric consultants (n=2, 50%) and residents (n=2, 40%) and medical interns (n=80, 100%).

The mean score of all the physicians who completed the questionnaire was: 14.21, SD 4.16 (45.8%) (*Table I*). The physicians performed best in questions pertaining to asthma diagnosis (63.7%, SEM 2.7) and scored poorly in questions regarding prevention of asthma triggers (29.5%, SEM 31). The pulmonary fellow got the highest mean score of 18.50, SD 3.82 (59.7%, SEM 12.3) followed by the consultant staff of the hospital with mean score of 58.7%, SEM 15.3. Questions pertaining to asthma diagnosis, pathology and pharmacology were the subject area where the fellows outscored their physician counterparts. The consultants, on the other hand, got higher mean scores in core asthma questions dealing with assessment, prevention, asthma classification and therapy. The medical intern obtained the lowest mean with 40.6%, SEM 10.3. The residents, on the other hand, were slightly above the overall score obtained. In the eight content subject of the NHLBI Global Initiative for Asthma Guidelines, the surveyed physicians did poorly in asthma assessment, education, prevention, severity classification and choice of appropriate therapy.

Significant differences were noted among the surveyed physicians according to the level of training in the subject areas of the guidelines pertaining to diagnosis, pathology, pharmacology, severity and therapy. This implies that the consultant staff of the hospital, the fellows-in-training, residents and medical interns differs in their knowledge and understanding of the guidelines. Probable reasons cited were the differences in the mode of obtaining the information, the lack of sufficient information drive for the clinical practice guidelines, and practice variation.

Looking into the percent score distribution among the different specialties the pulmonary specialists obtained the highest with 61.7%, SEM 11.6, followed by the medical internists with mean score of 54.4%, SEM 15.2. The eight core asthma questions where the pulmonary specialists got a higher score than their counterparts were: assessment, diagnosis, pathology, pharmacology, severity and therapy. The pediatricians had a mean score of 45.2%, SEM 5.9 and they performed better than the family physicians in questions dealing with asthma diagnosis and therapy. Low mean scores in subject areas of assessment, education and pathology were obtained.

The pattern of scores according to physicians' level of training did not change when the surveyed physicians were grouped into their respective specialties. In general, the core subjects that should be addressed in dissemination of asthma guidelines should give more attention to the importance of education, prevention, asthma severity classification and proper institution of therapy.

Significant differences were observed among the different specialties with respect to their knowledge of the guidelines for the following subjects: asthma diagnosis, assessment, pathology, pharmacology, prevention and therapy.

Discussion

Early epidemiologic studies on the prevalence of bronchial asthma in the Philippines are not specific. The Philippine Consensus Report on Asthma 1999 stated that the lack of consensus on the definition of asthma leads to a lack of uniformity in methodological and diagnostic practices. This partially explains the difficulty in developing studies to gather epidemiologic data on asthma. However, barely a decade after this report was released much has changed in the understanding of the pathophysiology and definition of bronchial asthma. Currently, the Philippine Consensus Report on Asthma 2004 updated its asthma definition to make it congruent with the Global Initiative for Asthma Report 2002, giving more emphasis on bronchial inflammation and hyper-responsiveness. With the framework, limited reports on the national prevalence of asthma were gathered showing a prevalence of 12% in children aged 13-14 and 17-22% in older age groups. It is noteworthy that over a quarter of the combined prevalence of the productive groups of our population has bronchial asthma. Hence much attention should be focused on addressing this controllable disease.

Clinical practice guidelines are one of the currently used strategies in the diagnosis and management of common diseases. The goal is to have a common ground in disease knowledge and understanding from evidence-based studies. In bronchial asthma, the NHLBI Global Initiative for Asthma 2002 and the Philippine Consensus Report 2004 both emphasized on the core asthma definition, symptomatology, assessment, diagnosis, education, prevention, asthma severity classifications and therapy. In this study, the Global Initiative for Asthma Report 2002 guideline was used because the latter was not yet published and not fully disseminated.

The results of the study showed that the overall knowledge and understanding of the physicians in the asthma guidelines is below the level found by Doershug et al,[3] which was 60%. It was even lower than the local study done among fellows and residents in a similar tertiary government hospital, which was 48%.[9] The

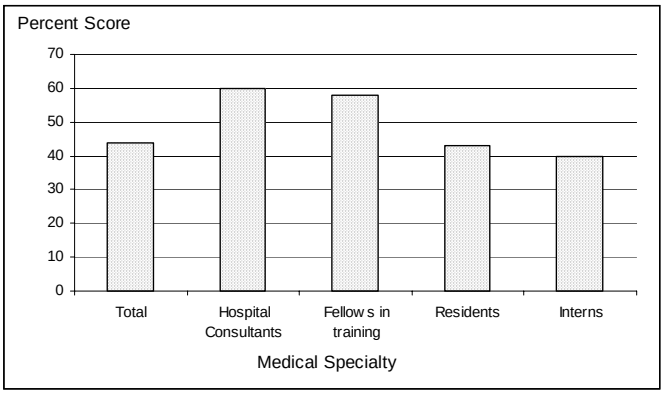

Figure 1 Mean performance scores of physicians to asthma classification of severity

pulmonary fellows performed better than consultants and residents primarily because understanding of the guidelines were thoroughly emphasized during conferences, case discussions and lectures. Similarly, with regard to specialties, the pulmonary medicine specialists ranked higher than the rest. But the results also showed that this group of physicians scored poorly in areas related to the importance of patient asthma education and trigger prevention.

Even more disturbing is the fact that the respondents did not properly classify the patients in question according to their asthma severity with a mean score of 44.5%, SEM 20.3 (*Figure 1*), findings that were similar to the studies of Doershug et al[3] (46%) and Reyes et al[9] (43%). Improper asthma classifications may also mean under-treatment or wrong choice of appropriate asthma therapy. The sequela of under-treatment is devastating to the patient. The patient may go into frequent asthma exacerbations leading to airway remodeling, which may later be unresponsive to any form of treatment and hence lead to fatal asthma.

Across the different specialties, pediatricians and family medicine practitioners differed in their understanding of the guidelines, particularly on asthma diagnosis, assessment, pathology, pharmacology, prevention and therapy. The reasons could be the differences in opinions with regard to the guideline components. Cabana et al[11] noted that pediatricians' adherence to asthma guidelines were between 39% and 53%. Barriers to non-adherence were noted for corticosteroid prescription, peak flow meter use and patient screening and counseling. Further, a survey done among physicians caring for asthmatic children reported that use of peak flow measurement was only 21% and less than 50% of them advised written care plans. Improvement were noted in specific areas such as written care plans, anti-inflammatory dosing and providing future follow-up.[6] Much improvement in adherence and understanding of asthma guidelines should consider the range of barriers that pediatricians face, such as lack of awareness, familiarity or agreement and external barriers to environmental, guideline or patient factors and the inertia of previous practice.[12]

In general, regardless of level of training and specialties, intensive effort towards guidelines education should be instituted, particularly in proper asthma assessment, trigger prevention, classification of asthma severity and treatment. The identified barriers mentioned may affect the outcome of good clinician education

Interventions that address these drawbacks could considerably enhance the extent to which physicians' clinical practices follow practice guidelines. It should be emphasized that employing clinical guidelines for asthma care consistent with national practices makes optimum the possibility of providing consistent and coordinated treatment among asthmatic patients.[13]

Effective implementation of clinical practice guidelines are influenced in many ways by education, financial incentives, management strategies, performance expectations and alteration of structural aspects of the clinical environment. But foremost among these is clinician education. Intervention strategies on clinica1 education are multilevel and multidisciplinary. The following are the means for an effective promotion and better understanding of clinical practice guidelines, as stated in a paper by Ockene and Zapka:[14]

1. Educational strategies in the form of information dissemination using traditional continuing medical education lectures, workshops, interactive curricula, videos, use of electronic technologies and other designs that aim to influence awareness, knowledge and attitudes toward guidelines and their recommendations.

2. Education in the context of other activities in the form of clinical applications of the knowledge obtained from lectures, and reinforcing it at every opportunity through return demonstrations to patients and other providers of health care. In this way, clinicians become asthma educators themselves.

3. Meet the challenges and recommendations for providing adequate education to promote guideline implementation. To meet this challenge, clinicians, irrespective of their specialties, form a part of an organization with the commitment and expectations geared toward a common goal of improved asthma care practices. An example is forming an asthma health care program that oversees the continuing education of specialists, residents, interns, nurses, other health care providers and patients themselves.

Conclusion

Knowledge and understanding of the NHLBI Global Initiative for Asthma Report 2002 of the physicians at VMMC were determined. The results showed that the overall knowledge and understanding of the surveyed physicians need further improvement, particularly in subject areas pertaining to assessment, asthma education, prevention, severity classification and treatment. Similarly the physicians differed in the same components as far as their understanding of the guidelines was concerned. Reasons for the differences were: lack of awareness of the guidelines, lack of familiarity with the guideline components and the factor of hospital practice variation. Clinician education through lectures, workshops, interactive modular instructions, return patient demonstrations and organizing an asthma management program across the different specialties, medical residents and interns of the hospital are the recommended strategies in improving outcome in asthma education.

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Validation of the American College of Chest Physicians (ACCP) Anatomic Diagnostic Protocol in the Evaluation and Management of Chronic Cough in the Immunocompetent Filipino Adult

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Background. Chronic cough, defined as cough persisting for at least three weeks, is a common diagnostic and therapeutic problem. A consensus panel report by the American College of Chest Physicians (ACCP) was published in 1998. Its applicability to the local setting has not been tested. No major study has addressed its etiologies in the Filipino patient.

Objectives. This study intended to determine the applicability of the ACCP Anatomic Diagnostic Protocol in the evaluation and management of chronic cough among immunocompetent Filipino adults, to determine the reasons and measure the effects of deviation(s) from the Protocol, if any, on the identification of the etiologies of chronic cough and the success of therapy, and to develop an algorithm with modifications of the ACCP Anatomic Diagnostic Protocol tailored to the local setting.

Materials and Methods. An ambispective study was conducted between January 2003 and December 2004 at the pulmonary clinics of the Philippine General Hospital and outpatient pay clinics of four pulmonary consultants who were holding their clinic near PGH. The subjects were adult patients of at least 18 years of age who consulted for cough of at least three weeks duration. Patients with immunocompromised states were excluded. A 19-item yes-or-no compliance checklist to assess adherence to the key components of the protocol was developed and pre-tested and each patient who could be evaluated was assessed independently by three board-certified pulmonologists. An overall compliance score for each patient is the sum of the number of items with a 'yes' response divided by the total applicable items. The assessment of compliance was the result of the concurrence of at least two pulmonologists.

Results. 284 patients were enrolled into the study. Fifty (17% of total subjects) were lost to follow up with 237 patients available for evaluation. 61.3% were females, with mean age of 50.18 $\pm$ 18.69 years. The mean duration of cough was 22.2 $\pm$ 55.64 weeks. The overall compliance rate to the key components of the ACCP protocol was 84 % ($\pm$ 11.71). Higher compliance rates were observed when the final diagnosis was pulmonary malignancy, pulmonary tuberculosis and ACE-induced cough and lowest for post-infectious cough. The compliance rates to the individual key components of the algorithm varied widely. The major deviations stemmed from the use of empiric drug therapy without confirmatory laboratory testing in 70% of patients and the use of non-specific cough therapy at the outset, even when a specific etiology had been identified, in 40% of patients. These deviations were highest among patients with GERD, PNDS and asthma.

Conclusions. The ACCP algorithm is generally applicable in the local setting. The overall mean compliance of pulmonologists practicing in a university teaching hospital was 84%. Higher compliance rates were observed when the final diagnosis was pulmonary malignancy, pulmonary tuberculosis and ACE-induced cough and lowest for post-infectious cough. The greatest deviations were noted among patients with ACE inhibitor-induced cough, GERD, PNDS and asthma. An algorithm was proposed in the evaluation and management of chronic cough. *Phil Journal of Chest Diseases. Vol. 14 No. 1 pp: 17-28*

Keywords: Chronic cough, Diagnosis, Management

Introduction

Cough is one of the most common symptoms for which patients seek medical attention from primary care physicians and pulmonologists.[1-3] Referrals of patients with persistently troublesome cough of unknown etiology has been shown to account for 10-35% of a pulmonologist's outpatient practice.[4]

Cough can be caused by a multiplicity of disorders. Estimating the duration of cough is crucial in narrowing the list of possible etiologic diagnosis. Presently, two published consensus panel reports are available for defining cough in terms of duration. The American College of Chest Physicians (ACCP) categorized cough as acute, lasting less than three weeks; or chronic, lasting three weeks or more. These two categories are not mutually exclusive.[4] The European Respiratory Society (ERS) defined chronic cough as more than eight weeks duration.[5] Irwin and Madison characterized cough as acute (lasting less than three weeks); subacute (lasting three to eight weeks, or chronic (persisting beyond eight weeks).[1]

Chronic cough is a challenging problem to practicing physicians.[1] There are at least a hundred disease etiologies to be considered. The cause of chronic cough can be determined in most adult patients. Specific therapy for chronic cough in a majority of patients is usually successful when it is evaluated in a systematic

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manner. In 1981, Irwin, et al proposed a systematic evaluation of chronic cough, which was based on the premise that each cough involves a complex reflex arc that begins with irritation of a receptor. Once started, it proceeds according to a fixed pattern. Impulses from these receptors are conducted to a central area by way of afferent nerves and are then passed down to appropriate efferent nervous pathways to expiratory musculature.[1] Irwin and his colleagues believed that a diagnostic approach that systematically evaluates locations of the afferent limb of the cough reflex for diseases that might be causing cough, and relating this to the patient's symptomatology, will lead to the determination of the specific etiology of the cough. Consequently, rational recommendations for targeted and successful therapy could then be made. In their first series employing the anatomic diagnostic protocol, they were able to determine the cause of chronic cough in all patients. They found that postnasal drip syndrome and/or bronchial asthma accounted for 72% of the cases. In terms of the diagnostic components of the protocol, the clinical history, physical examination, and methacholine inhalational challenge test together pinpointed the cause in 86% of the patients. More expensive or invasive investigations were necessary in only 14% of cases. Adjusted success rates for specific therapy, an average of 4.4 and 18.9 months after prescription, were 98 and 97%, respectively.[18]

Since then, the anatomic diagnostic protocol for chronic cough has been "validated" among immunocompetent patients in many prospective and retrospective cohort studies.[6-14] No study has been done to investigate its utility among immunocompromised subjects. Majority of these studies involved adults. In most of these studies, the cause was determined from 88 to 100% of the time, leading to successful therapy in 82 to 98% of the patients.[4] In two studies, the cause of cough was determined in only 55% and 78%. Cough was eliminated in only 68% in the latter study.[13-14] The difference in the results in these two studies were probably due to the different populations studied or to the use of different diagnostic and therapeutic protocols.

In 1998, the American College of Chest Physicians (ACCP) consensus panel adapted Irwin's approach and recommended the testing of its applicability in specific countries as a systematic algorithmic protocol both for the evaluation and management of chronic cough.[4] Its applicability to the Philippine setting has not been tested and the local pulmonologists' degree of adherence to the algorithm has not been measured.

The applicability of the protocol in the approach of the Filipino patient with chronic cough needs to be determined because it has components that may not be practical in the local setting. The cost of the diagnostic examinations incorporated in the anatomic diagnostic protocol is often beyond the reach of most Filipinos. Moreover, some of these investigations, including methacholine inhalational challenge test or esophageal pH monitoring are available only in selected tertiary centers. Consequently, practicing physicians may usually opt for nonspecific therapy or empiric specific therapy based on clinical grounds alone. Such management approaches may obviate the need for costly tests, yet may also consequently subject patients to potentially harmful or useless multiple medications, and may actually drive up the total cost.

Thus, this study aims to determine the applicability of the ACCP Anatomic Diagnostic Protocol in the evaluation and management of chronic cough among immunocompetent Filipino adults; to determine the reasons and measure the effects of deviation(s) from the Protocol, if any, on the identification of the etiologies of chronic cough and the success of therapy; and if necessary, to develop an algorithm with modifications of the ACCP Anatomic Diagnostic Protocol tailored to the local setting.

Materials and Methods

Study Design and Population. An ambispective study was conducted between January 2003 and December 2004 at the pulmonary clinics of the Philippine General Hospital (PGH) and outpatient pay clinics of the pulmonary consultants who were holding their clinic near PGH. The subjects were adult patients of at least 18 years of age who consulted for cough of at least three weeks duration. Patients with immunocompromised states such as the presence of known active malignancy, recent or ongoing chemotherapy and/or radiotherapy, suspected or diagnosed human immunodeficiency virus (HIV) infection or acquired immunodeficiency syndrome (AIDS), chronic intake of systemic steroids, and previously diagnosed with end-stage diseases including patients with chronic renal failure undergoing dialysis, those with uncontrolled diabetes or patients with chronic liver failure were excluded.

Study Procedure. *Figure 1* provides an outline of the general conduct of the study.

1. *Initial Assessment* At entry (First Visit), a medical history was taken and physical examination was performed by the fellow- or consultant-in-charge. General data were obtained including age, sex, complete address and contact numbers, marital status, occupation and history of smoking. The initial evaluation also included questions on the duration, frequency, timing,

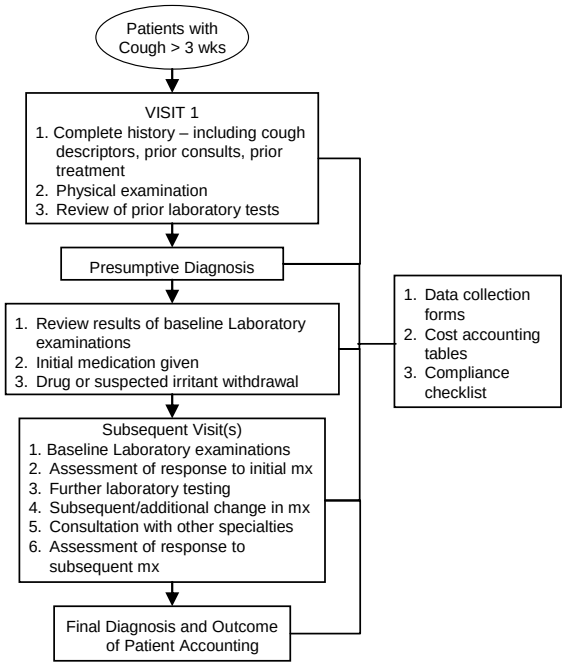

Figure 1. Study flow chart

character, and any recent worsening of cough; presence (viscosity, color and quantity) or absence of phlegm; any concomitant or associated complaints, e.g., dyspnea, chest pain or tightness, nasal symptoms, postnasal drip, throat complaints, epigastric pain and constitutional symptoms; history of an upper respiratory tract infection (URTI) or flu-like symptoms prior to or at the onset of cough; suspected or identifiable environmental irritants; intake of ACE-inhibitor drugs or other anti-hypertensive medications; known medical illness, including asthma and other lung diseases, allergic rhinitis, gastroduodenal pathologies, atopy, hypertension and cardiac illnesses, or any other co-morbidities; and a list of current medications. The patients were also probed in greater detail about the prior management of cough from its onset and up to the first visit, including previous medical consults, diagnostic studies and their results; intake of self-medicated and/or doctor-prescribed drugs for the cough, noting down the dose, dosing interval, duration of intake and the effect of therapy; and, any procedure undertaken to resolve the cough. When the physician-in-charge failed to record any of the previous information, attempts were made to ask the patient at a later time, during subsequent clinic follow-ups, updates by telephone or via home visits. Whenever possible, previous medical records of patients from other clinics were retrieved or their prior doctors contacted to verify their given information.

After the initial evaluation, a Presumptive Pre-Treatment Diagnoses (primary and differential Diagnoses) made by the physician-in-charge were recorded. The laboratory examination(s) and all the medication(s) he/she prescribed or withdrew on the first visit were likewise noted.

2. *Subsequent Follow-up(s)* Subsequent follow up information was obtained including the results of any laboratory examination(s) that were ordered at the first visit and in any of the subsequent visits; self-reported compliance, development of adverse events and response to initial management any change or addition of medications for the cough. noting down the drug, dose, dosing interval, self-reported compliance, actual duration of intake and the effect of therapy; withdrawal of medications; total number of pulmonary visits related to the current cough; and, referrals to other physicians or specialists, including the number of visits. The sequence by which the laboratory exams were ordered and the medications prescribed was likewise recorded. The type, number and prioritization of laboratory examinations ordered and the medications prescribed for any given patient were at the discretion of the attending physician; no attempt was made to influence his/her decision. Likewise, scheduling of follow-up visits was determined by the physician and the patient. If a patient, out of his own volition, decided to consult other physicians, the patient was interviewed on the diagnosis provided by the other physician as well as results of any additional laboratory test(s) that were ordered or carried out and details on the medications prescribed. Whenever possible, these physicians were likewise contacted.

3. *Final Outcome* The Final Diagnosis of Chronic Cough was determined by taking into consideration the results of the historical information, physical findings, laboratory examinations and the response to specific therapy directed at the identified etiology. Even if the findings from the first three criteria already highly suggested an etiologic diagnosis but information on the latter was not available, the final outcome (up to two months from the first visit) was still labeled as unknown. The final diagnosis of the cough is a reflection of the consensus assessment of at least two pulmonologists who independently assessed the data collection forms of each patient. The response of each patient to therapy was graded as: Complete Resolution of cough (complete disappearance of cough); Significant Improvement (cough still present but there was a notable decrease in frequency and severity and it was no longer disturbing or distressing); Minimal Improvement (some decrease in frequency and severity but cough was still disturbing or distressing); Absence of Improvement (same character as pretreatment descriptors); and, Worsening

(aggravation of cough compared to pre-treatment descriptors). The first two categories defined Treatment Success whereas the latter three categories were considered together as Treatment Failure. For patients whose cough completely resolved or significantly improved, the number of weeks needed to achieve the desired result was likewise determined. The response to therapy was a purely subjective assessment as graded by the patient. If the patient failed to follow up before an outcome could be definitively assessed, he/she was contacted by phone or via home visit. For this study the final outcome response to management was determined up to two months from the initial visit, during which time a note was made of the follow up status of each patient. Every attempt was made to contact all the patients entered into the study. Patients who were completely lost to follow up because of the absence of or wrong information on their contact telephone or mobile phone numbers, non-disclosure or provision of fictitious addresses, change of address or residence in areas outside of Manila were identified.

Operational Definitions

1. Presumptive Pre-Treatment Diagnostic Criteria- The following Criteria are established by the ACCP Consensus Panel in making a specific diagnosis for the known etiologies of cough. A comprehensive review of these conditions can be found in the report.[4] The following is a summary for the more common etiologies of chronic cough:

a. Postnasal drip syndrome (PNDS) is considered when: (1) patients describe the sensation of having something drip down into their throats, nasal discharge, and/or the need to frequently clear their throats, and/or (2) physical examination of the nasopharynges and oropharynges reveals mucoid or mucopurulent secretions and/or a cobblestone appearance of the mucosa; and, (3) rhinosinusitis is considered a potential cause of PNDS when sinus radiographs demonstrate more than 6 mm of mucosal thickening, air-fluid levels, or opacification of any sinus.

b. Bronchial Asthma is considered when: (1) patient complains of episodic wheezing, shortness of breath plus cough, and are heard to wheeze, or (2) reversible airflow obstruction is demonstrated by spirometry (FEV_1 increased at least 12% + absolute 200 ml increase from baseline after inhalation of two puffs of a short-acting bronchodilator, even in the absence of wheeze, or (3) a bronchoprovocation test is positive in the presence of normal routine spirometry and absence of wheeze, or (4) diurnal peak flow variability is at least 20%, in the presence of normal routine spirometry and absence of wheeze (5) The diagnosis of asthma is not made in any patient who experiences an obvious respiratory tract infection within two months prior to examination.

c. Gastroesophageal reflux disease (GERD) is considered when: (1) patients complain of heartburn and a sour taste in their mouths, or (2) upper gastrointestinal contrast roentgenograms demonstrate reflux of barium, or (3) 24-hour pH esophageal monitoring is abnormal, in the absence of upper gastrointestinal complaints.

d. Chronic Bronchitis is considered when: (1) cough and phlegm production are present on most days over a period of at least three months and for more than two consecutive years in a patient in whom other causes of chronic cough have been excluded, and, (2) the patient is known to smoke cigarettes or is exposed to industrial dust or fumes, and, (3) spirometry reveals airflow obstruction without bronchodilator reversibility.

e. Bronchiectasis is considered when: (1) cough with productive phlegm which is thick, tenacious and difficult to expectorate and becomes frankly purulent during an exacerbation; and, (2) chest radiographic changes are suggestive (e.g., crowded markings, increase in size and loss of definition of segmental markings; and/or, (3) high resolution CT scan of the chest confirms the diagnosis.

f. Post-infectious Cough is considered when: (1) cough occurs only after a respiratory tract infection; and, (2) a patient has normal chest radiograph; and, (3) other diagnoses have been excluded.

2. Post-treatment/Final Diagnostic Criteria - According to the ACCP consensus panel report, the final diagnosis of the cause of cough requires fulfillment of the presumptive diagnostic criteria and having the cough disappear or substantially improve as a complaint within two to four weeks of specific therapy directed at the identified cause. The following is a summary of the recommended treatment for the more common etiologies of chronic cough:

a. Cough due to PNDS Specific therapy for postnasal drip syndrome depended upon the etiology. Allergic, perennial non-allergic, post-infectious, environmental irritant and vasomotor rhinitis are treated predominantly with intranasal steroid, an antihistaminic decongestant preparation (dexbrompheniramine maleate plus d-isoephedrine) and, when feasible, avoidance of environmental precipitating factor(s). Vasomotor rhinitis that failed to respond to the above measures is treated with intranasal ipratropium bromide. Sinusitis is treated with a combination of antibiotic, decongestant nasal spray (oxymetazoline hydrochloride) and dexbrompheniramine maleate plus d-isoephedrine.

Table I. Characteristics of Patients Studied

Characteristics	Completed No. (%)[a]	Lost to Follow-up No. (%)[a]	Total No. (%)[a]	p-value
Actual No. of Patients	237 (82.6)	50 (17.0)	287 (100)	
Females	147 (62.8)	27 (54.0)	174 (61.3)	0.242
Age, years, mean (SD)	50.18 (18.69)	48.92 (17.76)	49.97 (18.51)	0.664
Ever smoked	57 (25.0)	(44.2)	76 (28.2)	0.010
Current smokers	15 (6.6)	8 (18.6)	23 (8.5)	0.016
History of atopy	35 (15.1)	5 (12.2)	40 (14.7)	0.629
History of prior lung Disease	55 (23.7)	13 (28.9)	68 (24.5)	0.529
With co-morbidities	74 (31.5)	14 (29.2)	88 (31.1)	0.751
Hypertension	38 (16.2)	9 (18.8)	47 (16.6)	0.661
Diabetes	12 (5.1)	5 (10.4)	17 (6.0)	0.141

[a] denominator used is number of valid responses

b. Cough due to Bronchial Asthma Asthma is treated with oral or inhaled steroids, and inhaled or oral bronchodilators.

c. Cough due to GERD GERD is treated with a high protein, low fat, anti-reflux diet, eating three meals a day, not eating or drinking for 2 to 3 hours prior to lying down except for taking medications, head of bed elevation, and a proton pump inhibitor for at least eight weeks.

d. Cough due to Chronic Bronchitis Chronic bronchitis is treated initially with cessation of smoking or the elimination of the irritant from the environment and inhaled anticholinergic drugs.

e. Cough due to Bronchiectasis Bronchiectasis is treated with antibiotics, chest physiotherapy and postural drainage, and theophylline and/or beta-agonists.

f. Post-infectious Cough Patients whose cough is protracted or persistently troublesome can be treated with a trial of a brief course of oral corticosteroid. An inhaled corticosteroid can be tried if tolerated and the cough is not severe. Ipratropium has also been shown to attenuate post-infectious cough. Antitussives can be added on occasions. Macrolide antibiotics are given for presumed mycoplasmal or chlamydial infections. In the case of presumed pertussis, treatment with a macrolide or trimethoprim/sulfamethoxazole is indicated.

Measurement of Compliance to the ACCP Anatomic Diagnostic Protocol

We developed a 19-Item Yes-or-No Compliance Checklist to assess adherence to the key components of the Protocol. The individual items of the ACCP algorithm were assumed to have equal weights. Any "yes" answer corresponds to a desirable response, as applicable, according to the presumed and final diagnosis(es). Three PCCP-certified pulmonologists independently evaluated the clinical records of each patient, blinded to the identity of the physician-in-charge. Their evaluations were tallied for each item. An overall compliance score for each patient was the sum of the number of items with a "yes" response divided by the total applicable items. The assessment of compliance for individual items and the overall compliance score is the result of the concurrence of at least two pulmonologists. The evaluation and management of patients who were lost to follow up was not included in the compliance assessment due to lack of complete information.

Statistical Analysis Data collection forms were developed and pre-tested. Data encoding was accomplished using *EpiInfo* version 6.04. Statistical analyses were performed using *EpiInfo* version 6.04 and *Stata 7*. Descriptive statistics such as frequencies, means (± SD), modes, medians, ranges, and percentile ranks were obtained. The 95% confidence intervals of the means of compliance were likewise calculated. Differences between groups were compared with *Student's t test* for two group analyses and ANOVA for more than two-group analyses of continuous variables, and *chi square* analysis, for categorical variables. All

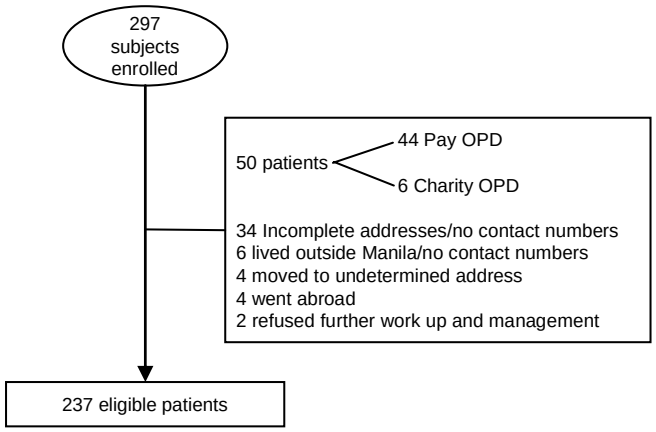

Figure 2 Patient accounting

Table II. Cough Description

Description	Completed No. (%)	Lost to Follow-up No. (%)	Total No. (%)	Chi-square p-value
Duration of cough, weeks, Mean (SD)	21.2 (52.06)	26.8 (70.64)	22.2 (55.64)	0.521[c]
Duration of cough, weeks, Mode (SD)	4.0 (52.06)	8.0 (70.64)	4.0 (55.64)	
Productive cough	139 (63.8)	16 (59.2)	155 (63.3)	0.647
Nocturnal cough	62 (31.2)	7 (46.7)	69 (32.2)	0.169[b]
Most common associated complaints				
Dyspnea	95 (40.8)	16 (37.2)	111 (40.2)	0.662
Chest pain	55 (23.7)	10 (23.3)	65 (23.6)	0.949
Nasal symptoms	57 (24.5)	6 (13.6)	63 (22.8)	0.116
Post-nasal drip	42 (18.4)	3 (7.5)	45 (16.8)	0.088
Throat complaints	101 (44.1)	13 (31.7)	114 (42.2)	0.139
Epigastric pain	9 (3.9)	2 (4.4)	11 (4.0)	0.558[b]
Constitutional symptoms	94 (40.2)	20 (41.7)	114 (40.4)	0.847
Recent worsening of cough	65 (27.5)	11 (23.4)	76 (26.9)	0.559
History of URTI prior to onset of Cough	47 (20.0)	7 (14.6)	54 (19.1)	0.384

a denominator used is number of valid responses
b Fisher's Exact Test
c T -test

tests were performed at level of significance, $p = 0.05$.

Sample Size Calculation Assuming compliance to the ACCP Anatomic Diagnostic Protocol is achieved in only 10% of patients and using the formula:

$N = [P(1-P)/CI^2] \times f(1-£)$

Where: N = number of patients with chronic cough to be studied

P = expected compliance rate

f(1-£) = square of the upper 12:£ point of the standard normal distribution at 95% CI = 3.84

CI = width of the interval

Thus:

$N = [10 (100-10)/ 25] \times 3.84 = 139$

Considering further a sampling design clustering effect of patients (to a specific physician) of 1.5 and multiplying this to the estimated sample size, the required number of subjects is 209. Finally, to cover for an estimated lost to follow up rate of 20%, the final minimum sample size should be 251.

Table III. Overall Mean Compliance and Mean Compliance by Frequency and Etiologic Diagnosis

Frequency and Type of Diagnosis	Mean	Mean Adjusted for Clustering (Standard Error)	95% Confidence Interval	ANOVA p-value
Overall Compliance	84.0	83.96 (1.54)	79.7,88.2	
Frequency of Diagnosis				*0.858*
One	83.6	83.6 (1.57)	79.3,88.0	
Two	84.9	84.9 (1.91)	79.6,90.2	
Three	84.2	84.2 (1.85)	79.0, 89.3	
Final Diagnosis				*<0.001*
Cough with Bronchial Asthma	83.6	84.4 (2.64)	77.1,91.8	
Post-.Nasal Drip Syndrome	82.4	82.4 (1.17)	79.1,85.6	
GERD	79.5	73.5 (0.00)	73.5, 73.5	
Bronchiectasis	87.3	87.3 (2.07)	81.5, 93.0	
COPD (Chronic Bronchitis)	84.6	84.6 (2.39)	77.9,91.2	
ACEI induced cough	89.1	89.1 (0.00)	89.1,89.1	
PTB	89.5	89.5 (1.10)	86.5, 92.6	
Pulmonary malignancy	92.5	92.5 (4.13)	81.0,103.9	
Post-infectious cough	76.7	76.7 (1.20)	73.4,80.0	
Others	82.6	82.6 (0.00)	82.6, 82.6	

Results

Of the 287 subjects enrolled in the study, 262 subjects (91%) consulted at the private clinic of the four pulmonologists and 25 patients (9%) consulted at the PGH charity out patient pulmonary clinics. Fifty patients (17%) were lost to follow up. Of these, six (12%) were charity patients. Thus, 24% of charity and 17% of pay patients with chronic cough dropped out from the study.

Figure 2 shows the summary of patient accounting.

Characteristics of the subjects are shown in *Table I*. The patients who could be evaluated (n=237) were comparable to those who were lost to follow up (n=50) except for the higher rate of smokers among the latter. The mean age was 50 years with predominance of females (61.3%). Twenty five percent had history of prior lung disease, usually tuberculosis. Thirty percent had other co-morbidities, the most common being hypertension and diabetes.

Table II shows a summary of the baseline cough characteristics. The mean duration of cough was 22.2 ± 55.64 weeks. Similarly, there was no difference in the

Table IV. `Over-All Compliance to Key Components of the ACCP Algorithm

Key Components	N	No.	%	Standard Error	95% CI
1 Was a clinical history and physical examination done at initial evaluation?	237	237	100.0	0.000	
2 Among patients suspected of ACEI-induced cough: Was the response to drug cessation assessed prior to further laboratory testing and start of drug therapy?	8	4	50.0	0.250	5.3 (94.7)
3 Was the response to drug cessation assessed for a minimum of 4 wks?	7	5	71.4	0.122	29.0 (96.3)
3a Was a chest radiograph ordered before any further laboratory testing and start of drug therapy?	230	212	92.2	0.038	87.9 (95.3)
4 Among patients with a n official chest radiograph and a suspected irritant, including cigarette smoking for current smokers, was the response to removal of the irritant assessed first prior to further laboratory testing and a start of drug therapy?	4	2	50.0	0.250	6.8 (93.2)
5 Among patients with an abnormal chest radiograph, was further laboratory testing done, when indicated, for the likely clinical possibility prior to specific treatment?	103	92	89.3	0.034	81.7 (94.5)
6 Was the presumptive diagnosis based on the criteria set by the Protocol?	237	237	100.0	0.000	
7 Among patients with a normal chest radiograph, were PNDS, asthma, GERD evaluated first, singly according to the order, or in combination, prior to evaluation of uncommon conditions?	90	88	97.8	0.011	92.2 (99.73)
8 For patients suspected of PNDS and have a productive cough, were four-view sinus radiographs ordered prior to beginning therapy, to check for sinusitis?	83	48	57.1	0.133	45.9 (67.9)
9 For patients suspected of PNDS, were sinus CT scans ordered much later in the evaluation?	6	4	66.7	0.222	22.3 (95.7)
10 Among patients suspected of asthma, was spirometry, bronchoprovocation challenge testing or peak now measurement and monitoring done before treatment?	107	72	67.3	0.164	57.5. 76.0)
11 Among patients suspected of GERD but do not have the typical upper GI symptoms, was a 24-hour esophageal monitoring or barium esophagography done prior to treatment?	7	2	28.6	0.247	3.7 (74.0)
12 Among patients with a suspected clinical condition, was a confirmatory laboratory testing done prior to drug therapy? Was empiric drug treatment withheld prior to full laboratory testing?	229	69	30.1	0.095	24.2 (36.5)
13 Was drug therapy for a specific etiology based on the recommendations of the Protocol?	232	227	97.8	0.009	95.0 (99.3)
14 Was the response of specific drug therapy assessed?	214	212	99.1	0.009	96.7 (99.9)
15 Among patients with multiple presumptive diagnoses, was drug therapy initiated sequentially? (in the same sequence that the abnormalities were discovered)?	109	107	98.2	0.017	93.5 (99.8)
16 Among patients with multiple presumptive diagnoses, was a partially successful therapy continued and other therapies sequentiallv added?	95	94	99.0	0.009	94.3 (100.0)
17 Was duration of specific treatment adequate to assess Clinical response?	214	212	99.1	0.008	96.7 (99.9)
18 Was non-specific therapy withheld at the outset (mucolytics, expectorants, cough suppressants)?	237	138	58.2	0.143	51.7 (64.6)

cough characteristics between patients who could be evaluated and those who were lost to follow up.

The longest duration of cough was 10 years, declared by two patients. More than 40% of subjects (41% of all subjects and 43% of the evaluated subjects) consulted for cough lasting for three to four weeks. Sixty-three percent of patients reported productive cough and about a third complained of nocturnal cough. Dyspnea, throat complaints and constitutional symptoms were common. Almost 30% of the patients noted worsening cough prior to consultation. Two out of ten patients reported symptoms consistent with an upper respiratory tract infection prior to or at the onset of cough.

Compliance to the ACCP Anatomic Diagnostic Protocol

The overall mean compliance rate to the key components of the ACCP anatomic diagnostic algorithm was 84% (95% CI: 79.7, 88.2), as shown in *Table III*. The design effect of clustering in the estimation of the overall compliance was calculated and it was determined to be 4.88; this was higher than the assumed clustering effect of 1.5 when the sample size was estimated. Nevertheless, when the overall mean compliance, the compliance rate per disease cause and the compliance rate according to the number of etiologies of chronic cough were adjusted for clustering effect, their results did not change significantly and exhibited relatively narrow 95% confidence intervals (*Table III*). There was no significant difference in the overall compliance among patients with one, two or three etiologies for the cough.

Despite the underestimated design effect, the study was able to detect differences in compliance across etiologies and across the key components of the ACCP algorithm. As shown also in *Table III*, among patients with single etiologies for their cough, the overall compliance rate of the evaluation and management was

Table V. Compliance to Key Components by Frequency of Final Diagnoses

Key Components		1 No. (%)	2 No. (%)	3 No. (%)
1	Was a clinical history and physical examination done at initial evaluation?	160 (100.0)	70 (100.0)	6 (100.0)
2	Among patients suspected of ACEI-induced cough: Was the response to drug cessation assessed prior to further laboratory testing and start of drug therapy?	3 (60.0)	0(0.0)	1 (100.0)
3	Was the response to drug cessation assessed for a minimum of 4 wks?	3 (75.0)	1 (50.0)	1 (100.0)
4	Was a chest radiograph ordered before any further laboratory testing and start of drug therapy?	138 (90.2)	67 (95.7)	6 (100.0)
5	Among patients with a n official chest radiograph and a suspected irritant, including cigarette smoking for current smokers, was the response to removal of the irritant assessed first prior to further laboratory testing and a start of drug therapy?	2 (66.7)	0 (0.0)	0 (0.0)
6	Among patients with an abnormal chest radiograph, was further laboratory testing done, when indicated, for the likely clinical possibility prior to specific treatment?	53 (86.9)	36 (94.7)	3 (75.0)
7	Was the presumptive diagnosis based on the criteria set by the Protocol?	160 (100.0)	70 (100.0)	6 (100.0)
8	Among patients with a normal chest radiograph, were PNDS, asthma, GERD evaluated first, singly according to the order, or in combination, prior to evaluation of uncommon conditions?	6 (98.4)	23 (95.8)	2 (100.0)
9	For patients suspected of PNDS and have a productive cough, were four-view sinus radiographs ordered prior to beginning therapy, to check for sinusitis?	27 (65.9)	18 (47.4)	2 (50.0)
10	For patients suspected of PNDS, were sinus CT scans ordered much later in the evaluation?	2(66.7)	1 (20.0)	0(0.0)
11	Among patients suspected of asthma, was spirometry, bronchoprovocation challenge testing or peak now measurement and monitoring done before treatment?	38 (62.3)	31 (72.1)	3 (100.0)
12	Among patients suspected of GERD but do not have the typical upper GI symptoms, was a 24-hour esophageal monitoring or barium esophagography done prior to treatment?	a (0.0)	1(33.3)	1 (100.0)
13	Among patients with a suspected clinical condition, was a confirmatory laboratory testing done prior to drug therapy? Was empiric drug treatment withheld prior to full laboratory testing?	48 (31.4)	21 (30.4)	0 (0.0)
14	Was drug therapy for a specific etiology based on the recommendations of the Protocol?	151 (96.8)	69 (100.0)	6 (100.0)
15	Was the response of specific drug therapy assessed?	139 (98.6)	66 (100.0)	6 (100.0)
16	Among patients with multiple presumptive diagnoses, was drug therapy initiated sequentially? (in the same sequence that the abnormalities were discovered)?	40 (95.2)	60 (100.0)	6 (100.0)
17	Among patients with multiple presumptive diagnoses, was a partially successful therapy continued and other therapies sequentiallv added?	33 (97.1)	54 (100.0)	6 (100.0)
18	Was duration of specific treatment adequate to assess Clinical response?	142 (l00.0)	64 (98.5)	6 (l00.0)
19	Was non-specific therapy withheld at the outset (mucolytics, expectorants, cough suppressants)?	94 (58.8)	41 (58.6)	3 (50.0)

highest for patients with pulmonary malignancy, PTB and ACE inhibitor induced cough. It was lowest for patients with post infectious cough, with the use of non-specific therapy at the outset as the most common deviation.

The compliance rate (% mean, SE and 95% CI) to the individual components of the ACCP anatomic diagnostic algorithm, as applicable; can be viewed in *Table IV*. Clinical history and physical examination was done for all patients. Similarly, the presumptive diagnosis was adjudged appropriate for all. A baseline chest radiograph was ordered for 92% of the patients who did not have one. Drug therapy for a specific etiology was determined to be based on the recommendations of the protocol in 98% of patients. Among patients with a normal chest radiograph, asthma and PNDS were usually among the top diagnoses initially considered. Among patients with an abnormal chest radiograph, further laboratory tests were performed, when indicated, in 89% of the patients. The response of specific drug therapy was evaluated and the duration of specific treatment was adequate to assess clinical response in 99%. Among patients with multiple presumptive diagnoses, drug therapy was initiated sequentially (in the same sequence that the abnormalities were discovered) and a partially successful therapy was continued and other therapies sequentially added in 99%.

As shown also in *Table IV*, the greatest deviations were notable among patients with ACE inhibitor induced cough, GERD, PNDS and asthma. The response to ACE inhibitor cessation was assessed prior to further laboratory testing and start of drug therapy for other conditions in only 50%. And in 30% of patients, the observation period for the response to drug cessation was less than four weeks.

The majority of patients with asthma, PNDS and GERD were treated empirically. Doctors ordered paranasal sinus radiographs in less than half of the patients with productive cough and suspected PNDS. In two of six patients, sinus CT scans were ordered at the outset without the benefit of PNS radiographs. Objective measures of lung function (most commonly peak flow measurement) were done in only 67% of asthmatic patients. No bronchoprovocation challenge test was performed since this was not available during the study period. Only two of seven patients suspected of GERD but didn't manifest with typical symptoms had objective confirmation through gastroscopy. Twenty four hour-

esophageal pH monitoring was not available throughout the study period.

In all patients with a suspected clinical condition, confirmatory laboratory testing done prior to drug therapy and withholding empiric drug treatment prior to full laboratory testing were achieved in only 30% of patients.

Non-specific therapy for cough was given early on, usually in consonance with therapy directed at a specific etiology, in 42% of patients.

Four patients had a normal chest radiograph and a suspected irritant. In only two patients was the response to removal of the irritant assessed first prior to further laboratory testing and start of drug therapy. One patient was found to have beta-blocker induced asthma; cough resolved with withdrawal of the drug and without the benefit of treatment. One patient who was a current smoker was enrolled in a smoking cessation program and a fixed combination steroid + beta-2 agonist inhaler was started for the residual cough. Two patients, both asthmatics, reported worsening of symptoms at particular settings; in one patient, this was observed since construction work was being done near her house and in the other, at work in a salmon factory. The latter two patients were prescribed asthma medications immediately although advice on control of triggers was also given.

Table V compares the compliance rate to the individual components according to the frequency of final diagnosis. No signification variation was noted.

Proposed Revised Algorithm Tailored to Local Needs and Problems

Figure 3 shows the proposed algorithm in the evaluation and management of chronic cough in the immunocompetent Filipino adult. Its development took into consideration the aforementioned results and findings of new literature published recently. The proposed revisions to the ACCP anatomic diagnostic algorithm are expected to make the new algorithm more useful and practical in the local setting.

Discussion

This study is the first major attempt to investigate immunocompetent Filipino adult patients with chronic cough. To our knowledge, it is the first study to measure directly the compliance of pulmonary specialists to a standard of evaluation and management that has been in existence since 1981 and was adapted by the ACCP consensus pane1.[4,18] At the time the study was initiated, no other consensus recommendations were available.

The overall mean compliance rate of the participating pulmonologists to the key components of the ACCP Anatomic Diagnostic Protocol was assessed to be generally good (84% ± 12%; 95% CI: 79.7, 88.2). As mentioned previously, even when adjusted for clustering effects, this did not change significantly. The compliance according to individual diagnoses, as can be gleaned from their 95% confidence intervals in *Table III*, showed fair to excellent ratings.

High marks were given for the conduct of the clinical examination, appropriateness of the basis for the presumptive diagnoses, the prescribed drug therapy for a specific etiology and the evaluation of specific treatment, and the adequacy of clinical response assessment. When applicable, baseline chest radiographs were ordered in 92% of patients. The conduct of proceeding across the evaluation and management of multiple presumptive diagnoses was also assessed to be highly appropriate.

The major deviations from the individual key recommendations of the ACCP algorithm mainly stemmed from the lack of confirmatory laboratory testing prior to drug treatment (that is, in 70% of patients who needed drug therapy, this was given empirically without the benefit of diagnostic tests) and the use of nonspecific cough therapy at the outset, even when a specific etiology had been identified. The latter was observed in 40% of patients. These departures from the recommended standard were usually seen in patients with GERD, PNDS and asthma.

An easily verifiable possible explanation for the lack of confirmatory laboratory testing being ordered is the unavailability of certain diagnostic tests locally during the study period, including bronchoprovocation test and 24 hour-esophageal pH monitoring. Based on clinical experience, we also intuit most patients, whenever possible, would request for empiric drug treatment and proceed only to laboratory testing if there is a lack of clinical response. Our results with laboratory testing in this study seem to support this belief. Fewer tests were actually done compared to those ordered, particularly if the test was expensive or their conduct was perceived to be inconvenient to the patient (e.g., screening CT of the sinuses, sputum AFB smears, spirometry). On the other hand, it is surprising to note that a simple bedside test to objectively assess lung function, like peak flow monitoring, was also not frequently performed in the clinics of the participating pulmonary specialists.

Even when performed, many of the tests recommended by the ACCP protocol have been shown to possess limited diagnostic utility in recent studies. Majority of asthmatics have been found to have normal

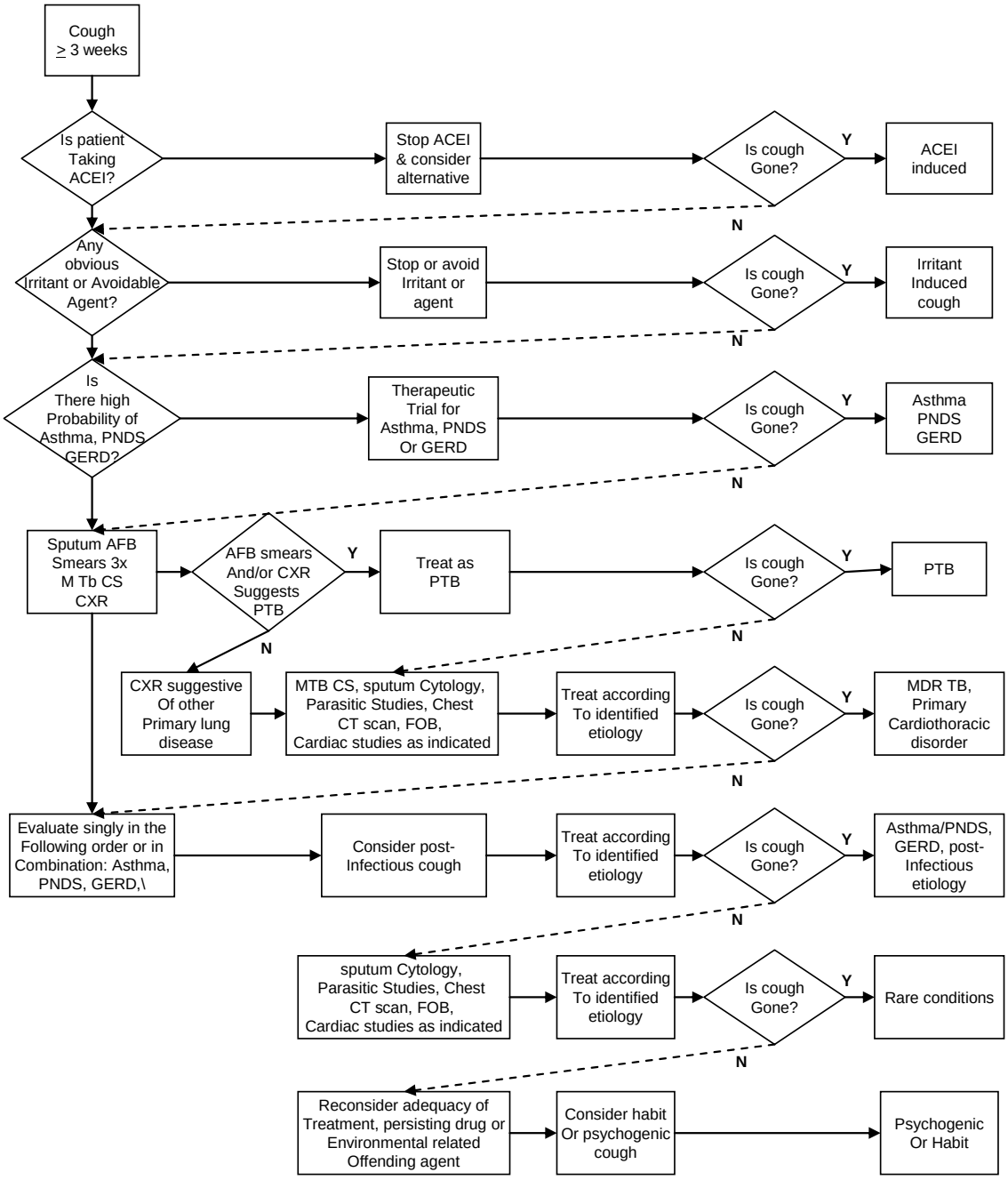

Figure 3. Proposed algorithm for the evaluation and management of chronic cough

spirometry and do not exhibit acute bronchodilator response, even when the patient is symptomatic.[19] A negative bronchoprovocation test does not rule out subsequent response to a trial of oral or inhaled steroids.[20] Even the value of peak expiratory flow measurements in documenting reversible airflow obstruction during the diagnostic work up of primary care patients with persistent cough has been questioned.[21] Pratter, et. al. have noted that, among patients with chronic cough, mucosal thickening seen during sinus imaging lacked specificity in diagnosing sinusitis and recommended delaying the performance of the test until after efforts at treating rhinitis have failed.[22] Fiberoptic bronchoscopy has been found to have a low yield in the diagnosis of refractory cough, adds little to the diagnosis in the context of normal or non-localizing chest radiographic or CT findings, and did not result in successful treatment alteration.[23-24]

Esophageal pH monitoring has also been found to be of limited value in the diagnosis of "reflux cough."[25] Poe and Kallay have shown that among their patients

with GERD, an empiric therapeutic trial with a proton-pump inhibitor with or without a prokinetic agent was successful in diagnosing and resolving cough in four of five patients and that in only a few patients was esophageal pH monitoring necessary to confirm the diagnosis.[26]

The value of empiric specific drug therapy in both diagnosing and treating chronic cough was assessed in a very recent study. Kastelik, et. al. developed a novel algorithm which utilized a clinical assessment of disease probability in order to determine whether to initiate treatment or investigate further. They prospectively applied the algorithm to 131 patients with cough lasting more than eight weeks. They found that empirically treating patients with a high clinical probability of asthma, PNDS and GERD before proceeding to further investigations resulted in identification of the cause of cough in 93% of patients and successful treatment was possible in the large majority of their patients. 26% of their patients were managed successfully without the need for any form of investigation other than chest radiography and spirometry.[27]

Many of our patients had historical descriptors that often led to a correct presumptive diagnosis. These included associated complaints, past medical history, experience with past treatments and the results of prior laboratory tests. This was probably why, in a significant number of patients, the participating pulmonologists opted for empiric drug therapy rather than conducting a more comprehensive diagnostic investigation prior to treatment. In essence, our practice seems to be akin to the probability-based algorithm of Kastelik and resulted in successful treatment in the majority of patients despite the lack of extensive confirmatory tests.

Lin, et. al. has shown that sequential empiric treatment may provide the cheapest option but had the longest treatment duration. On the other hand, strict adherence to protocols like that of the ACCP algorithm was the most expensive, but had the shortest treatment duration.[28] Hence, the challenge is to balance the cost with time to treatment success, without causing significant adverse events.

In recognition of the above considerations, a new algorithmic protocol was recently published by an ERS Task Force. The guidelines suggested two pathways, one using an empirical approach and the other one using the recommended investigations, and the reader is advised to consider these strategies in parallel.[5] The development of the proposed local algorithm heeded the recommendations of both the ACCP and ERS consensus panel reports.

One disturbing practice of the participating pulmonologists is the use of non-specific cough therapy in 40% of patients, while awaiting the results of a laboratory examination or in combination with medications directed at a specific cause. Although no significant adverse events were reported by our patients and such practice did not influence treatment outcome, this would obviously increase the total cost of treatment and has been found to have no therapeutic value, except in patients with significant structural lung disease or terminal pulmonary conditions.[4]

Conclusion

Two hundred eighty seven patient-encounters were included in this study. The lost to follow up rate was 17%. Two-thirds of the patients were females with a mean age of 50 years and mean duration of cough of 22.2 ± 55.64 weeks.

The ACCP algorithm is generally applicable to the local setting. The overall mean compliance of pulmonologists practicing in a university teaching hospital was 84%. This was not influenced by the frequency of identified etiologies per patient. Higher compliance rates were observed when the final diagnosis was pulmonary malignancy, pulmonary tuberculosis and ACE inhibitor-induced cough and lowest for post-infectious cough. The compliance rates to the individual key components of the algorithm varied widely. The greatest deviations were noted among patients with ACEI-induced cough, GERD, PNDS and asthma. The lack of compliance is traced to the practice of empiric drug therapy in the absence of confirmatory laboratory testing and the use of nonspecific cough therapy at the outset.

In the development of an algorithm more suited to the local setting, pulmonary tuberculosis should be considered at the outset. Empiric drug therapy when there is a high clinical suspicion for asthma, postnasal drip syndrome or gastroesophageal reflux disease is acceptable.

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The Economic Cost of the Evaluation and Management of Chronic Cough in the Filipino Adult

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Background Cough is undoubtedly one of the most common and debilitating symptoms found in all faces of chronic airway disease. Its impact on health is substantial. A few studies have been published regarding the economic cost of evaluating and managing chronic cough. None has been done in our country.
Objectives. It was the objective of this study to determine the cost of diagnosing and treating chronic cough in the adult Filipino and to calculate the cost of self-management practices and health-seeking patterns of patients with chronic cough.
Materials and Methods. An ambispective study was conducted among patients who consulted/were referred at the pulmonary clinics and out patient pay clinic of four pulmonary consultants. The study period was January 2003 until December 2004. The following are the inclusion criteria: patients of at least 18 years of age; cough of at least three weeks duration as the major reason of consultation or referral and patients should be immunocompetent. Immunocompromised patients were excluded.
Results. A total of 287 subjects were entered into the study. Fifty patients (17% of total subjects) were lost to follow up. 237 subjects remained evaluable for the economic analysis. On the average, each patient spent P 6,569.81 (95% CI: 5,789.26, 7,350.36) while seeking relief for chronic cough. Two-thirds of this amount was due to expenses incurred from drug therapy (P4,233.82). A patient spent a mean P4,327.37 (95% CI: 3,977.44, 4,677.29) during the study period. The most ex-pensive individual etiologic diagnoses, as expected, were chronic and terminal diseases, including pulmonary malignancy (P5,265.65), tuberculosis (P5,228.43), COPD (P4,706.66) and bronchiectasis (P4,2l6.30). A failed treatment was more expensive than a successful therapy (P6,468.51 vs. P8,651.02).
Conclusions. On the average, a Filipino immunocompetent patient will spend P 6,569.81 while seeking relief for chronic cough. Two-thirds of this amount is due to expenses incurred from drug therapy (P4,233.82). A failed treatment is more expensive than a successful therapy. *Phil Journal of Chest Diseases. Vol. 14, No. 1 pp: 29-39*

Keywords: Cough, diagnosis, therapy

Introduction

Cough is undoubtedly one of the most common and debilitating symptoms found in all faces of chronic airway disease. It is a common diagnostic and therapeutic problem. Cough is caused by a multiplicity of disorders and duration is important in determining the possible etiology of cough. At present, two published consensus reports are available for defining cough in terms of duration. The American College of Chest Physicians (ACCP) considered chronic cough as one "lasting three to eight weeks or longer," and thus, a cough of a shorter duration is deemed acute.[1] On the other hand, a task force convened by the European Respiratory Society (ERS) defined chronic cough as one of more than eight weeks dumtion.[2]

The exact prevalence at present is difficult to estimate. Recurrent cough is reported in 3-40% of the population.[3] Persistently troublesome chronic cough of unknown etiology has been shown to account for 10-30% of a pulmonologist's outpatient pmctice.[1]

The impact of cough on health is substantial. It can be an important defense mechanism which helps clear excessive secretions and foreign materials from the airways or as a symptom of an underlying disorder should also be considered as an important factor in the spread of infection and it is important to recognize its impact on health, in terms of the personal and economic cost to the patients.[1] In the United States, the annual cost of *treating* cough exceeds one billion.[4] An economic evaluation by Nadri in India showed that the average cost of treating chronic cough per patient using a modified anatomic diagnostic protocol was Rs 875.80 (US$ 18.30) and that 90% of patients were diagnosed with < Rs 1000.[5]

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A few studies have been published regarding the economic cost of evaluating and managing chronic cough. None has been done in our country. The cost of self-management practices and health-seeking pattern~ of such patients has not been measured.

Because of the limited information on the economic cost of evaluation and management of chronic cough in our country, it was therefore the objective of this study to determine the cost of diagnosing and treating chronic cough in the adult Filipino and to calculate the cost of self-management practices and health-seeking patterns of patients with chronic cough.

Materials and Methods

Study Population The study was conducted among patients who consulted/were referred at the pulmonary clinics and out patient pay clinic of four pulmonary consultants. The study period was January 2003 until December 2004. The following are the inclusion criteria: patients of at least 18 years of age; cough of at least three weeks duration as the major reason of consultation or referral and patients should be immunocompetent. Immunocompromised patients such as those known to have an active malignancy, recent or ongoing chemotherapy and/or radiotherapy, suspected or diagnosed human immunodeficiency virus (HIV) infection or acquired immunodeficiency syndrome (AIDS), chronic intake of systemic steroids, and previously diagnosed end-stage diseases including patients with chronic renal failure undergoing current dialysis, uncontrolled diabetes or patients with chronic liver failure were excluded.

Study Design The study design is ambispective; that is, data on the characteristics of cough, prior consults, treatment and expenses incurred were collected retrospectively or were available from records and then the cohort was followed up, taking into consideration the diagnostic modalities done, response and compliance to treatment and expenses subsequently incurred.

Study Procedure *Figure 1* provides an outline of the general conduct of the study.

Initial Assessment At entry (First Visit), a medical history was taken and physical examination was performed by the fellow- or consultant-in-charge. General data was obtained including age, sex, complete address and contact numbers, marital status, occupation and history of smoking. The initial evaluation also included questions on the duration, frequency, timing, character, and any recent worsening of cough; presence (viscosity, color and quantity) or absence of phlegm production; any concomitant or associated complaints, e.g., dyspnea, chest pain or tightness, nasal symptoms,

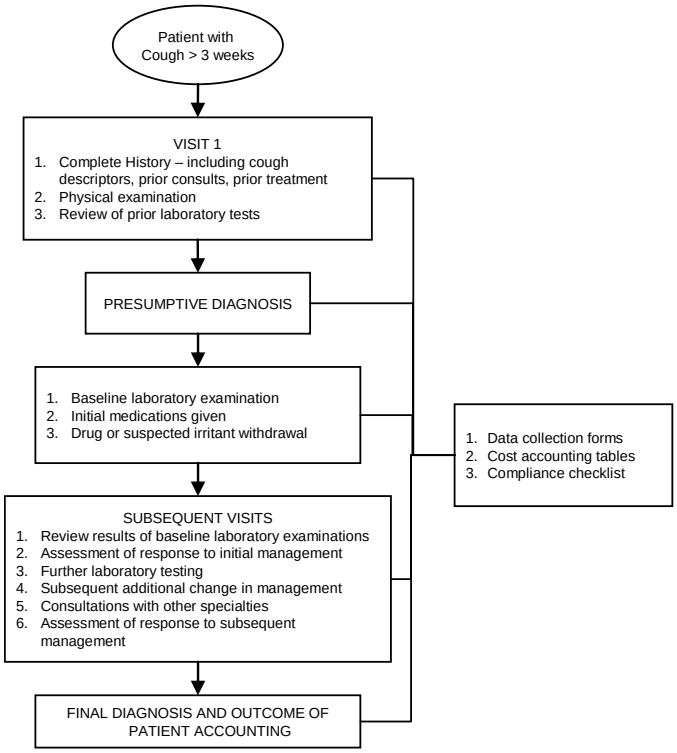

Figure 1 Study flowchart

postnasal drip, throat complaints, epigastric pain and constitutional symptoms; history of an upper respiratory tract infection (URTI) or flu-like symptoms prior to or at the onset of cough; suspected or identifiable environmental irritants; intake of ACE inhibitor drugs or other anti-hypertensive medications; known medical illness, including asthma and other lung diseases, allergic rhinitis, gastroduodenal pathologies, atopy, hypertension and cardiac illnesses, or any other co-morbidities; and a list of current medications. The patients were also probed in greater detail about the prior management of cough from its onset and up to the first visit, including previous medical consults, diagnostic studies and their results; intake of self-medicated and/or doctor-prescribed drugs for the cough, noting down the dose, dosing interval, duration of intake and the effect of therapy; and, any procedure undertaken to resolve the cough. When the physician-in-charge failed to record any of the previous information, attempts were made to ask the patient at a later time, during subsequent clinic follow ups, updates by telephone or via home visits. Whenever made of the follow up status of each patient. Every attempt was made to contact all the patients entered into the study. Patients who were completely lost to follow up because of the absence of or wrong information on their contact telephone or mobile phone

numbers, non-disclosure or provision of fictitious addresses, change of address or residence in areas outside of Manila were identified.

Operational Definitions

Presumptive Pre-Treatment Diagnostic Criteria- The following Criteria are established by the ACCP Consensus Panel in making a specific diagnosis for the known etiologies of cough. A comprehensive review of these conditions can be found in the report.[6] The following is a summary for the more common etiologies of chronic cough:

Postnasal drip syndrome (PNDS) is considered when patients describe the sensation of having something drip down into their throats, nasal discharge, and/or the need to frequently clear their throats, and/or physical examination of the nasopharynges and orpharynges reveals mucoid or mucopurulent secretions and/or a cobblestone appearance of the mucosa; and, rhinosinusitis is considered a potential cause of PNDS when sinus radiographs demonstrate more than 6 mm of mucosal thickening, air-fluid levels, or opacification of any sinus.

Bronchial Asthma is considered when patient complains of episodic wheezing, shortness of breath plus cough, and are heard to wheeze, or reversible airflow obstruction is demonstrated by spirometry (FEV_1 increased at least 12% + absolute 200 ml increase from baseline after inhalation of two puffs of a short-acting bronchodilator, even in the absence of wheeze), or a bronchoprovocation test is positive in the presence of normal routine spirometry and absence of wheeze, or diurnal peak flow variability is at least 20%, in the presence of normal routine spirometry and absence of wheeze.

The diagnosis of asthma is not made in any patient who experiences an obvious respiratory tract infection within two months prior to examination.

Gastroesophageal reflux disease (GERD) is considered when patients complain of heartburn and a sour taste in their mouths, or upper gastrointestinal contrast roentgenograms demonstrate reflux of barium, or 24-hour pH esophageal monitoring is abnormal, in the absence of upper gastrointestinal complaints.

Chronic Bronchitis is considered when cough and phlegm production are present on most days over a period of at least three months and for more than two consecutive years in a patient in whom other causes of chronic cough have been excluded, and, the patient is known to smoke cigarettes or is exposed to industrial dust or fumes, and, (3) spirometry reveals airflow obstruction without bronchodilator reversibility.

Bronchiectasis is considered when: (l) cough with productive phlegm which is thick, tenacious and difficult to expectorate and becomes frankly purulent during an exacerbation; and, (2) chest radiographic changes are suggestive (e.g., crowded markings, increase in size and loss of definition of segmental markings; and/or, (3) high resolution CT scan of the chest confirms the diagnosis.

Postinfectious Cough is considered when: (l) cough occurs only after a respiratory tract infection; and, (2) a patient has normal chest radiograph; and, (3) other diagnoses have been excluded.

Post-treatment Final Diagnostic Criteria - According to the ACCP consensus panel report, the final diagnosis of the cause of cough requires fulfillment of the presumptive diagnostic criteria and having the cough disappear or substantially improve as a complaint within two to four weeks of specific therapy directed at the identified cause. The following is a summary of the recommended treatment for the more common etiologies of chronic cough:

Cough due to PNDS

Specific therapy for postnasal drip syndrome depended upon the etiology. Allergic, perennial nonallergic, post infectious, environmental irritant, and vasomotor rhinitis are treated predominantly with intranasal steroid, an antihistaminic decongestant preparation (dexbrompheniramine maleate plus D-isoephedrine) and, when feasible, avoidance of environmental precipitating factor(s). Vasomotor rhinitis that failed to respond to the above measures is treated with intranasal ipratropium bromide. Sinusitis is treated with a combination of antibiotic, decongestant nasal spray (oxymetazoline hydrochloride) and dexbrompheniramine maleate plus D-isoephedrine.

Cough due to Bronchial Asthma

Asthma is treated with oral or inhaled steroids, and inhaled or oral bronchodilators.

Cough due to GERD

GERD is treated with a high protein, low fat, antireflux diet, eating three meals a day, not eating or drinking for 2 to 3 hours prior to lying down except for taking medications, head of bed elevation, and a proton pump inhibitor for at least eight weeks.

Cough due to Chronic Bronchitis

Chronic bronchitis is treated initially with cessation of smoking or the elimination of the irritant from the environment and inl1aled anticholinergic drugs.

Cough due to Bronchiectasis

.Bronchiectasis is treated with antibiotics, chest physiotherapy and postural drainage, and theophylline and/or beta-agonists.

Postinfectious Cough

Patients whose cough is protracted or persistently troublesome can be treated with a trial of a brief course of oral corticosteroid. An inhaled corticosteroid can be tried if tolerated and the cough is not severe. Ipratropium has also been shown to attenuate postinfectious cough. Antitussives can be added on occasions. Macrolide antibiotics are given for presumed mycoplasmal or chlamydial infections. In the case of presumed pertussis, treatment with a macrolide or trimethoprim/ sulfamethoxazole is indicated.

Economic Evaluation

Determination of Costs and Assumptions. A partial economic evaluation was performed, involving cost descriptions only, from the point of view of the patient? However, for the charity patients seen at the PGH outpatient clinics, hospital costs were also measured to take into account the hidden costs of the free consultation.

The Total Cost incurred is the sum of the Direct Cost and Indirect Cost. The Direct Cost is the actual costs borne by the patient and! or his family while in the process of seeking relief for his/her cough; this comprises out-of-pocket expenses relating to consultation with medical professionals and other health care givers; laboratory examinations and medical interventions undertaken; travel expenses; and drug therapy. The Indirect Cost is the cost that is borne by the patients in the form of minimum loss of productivity or opportunity costs. In this study, we considered the cost of time lost from work. We set a time limit for cost monitoring of up to two months from the first visit. Patients who failed to follow up within two months from the time of the first visit were interviewed by phone or during home visit(s) regarding any additional costs incurred, as described above.

Much of the aforementioned information was based on recall; thus, our results were significantly limited by the patients' ability to remember details of their care and their willingness to volunteer their history. Therefore, our results could very well underestimate the true cost of chronic cough. This is particularly true for patients with long standing cough of many months or years duration. We attempted to rectify these problems by undertaking more objective assessment of costs and declaring assumptions on their calculations, as detailed below. The total cost per patient described in the study must also be regarded as the minimum average cost. Patients who were lost to follow up were not included in the cost analysis due to lack of complete information.

Cost of Consults The patients were asked regarding consultations undertaken while seeking relief, from the onset of the cough until the first visit to the participating pulmonologist and all subsequent consultations within the two-month study period. These consultations included any visit to a general or family physician (GP/FP), internist, a specialist, *herbolario,* alternative medicine practitioner and/or other health care givers. The professional fees paid were recorded. When a patient did not recall how much was paid, if the doctor was known to us, we contacted the latter and asked how much he/she would have charged for such an encounter. We computed the mean declared cost per consult for each type of physician and used this as the input for those visits where a patient could not recall the doctor charges.

The fees charged from the first visit with a subject pulmonologist to the subsequent visits were directly determined. The amount recorded per visit is the mean amount charged by all four pulmonologists during the year of consultation. We also noted fees charged for referrals to other specialists or other health professionals. We assumed that all encounters were charged.

The patients who consulted at the charity clinics of PGH did not pay professional fees. These were calculated as hospital costs.

Diagnostic Cost We attempted to account for expenses paid for all laboratory examinations related to the workup of a patient's cough, from its onset up to two months after the first visit for the study. If the patient could not recall the exact amounts paid, we contacted the laboratories or hospitals concerned. If these could not be contacted, we assumed the outpatient pay rates of PGH. For patients seen at the PGH OPD pulmonary clinics, the rates were based on the outpatient charity rates. Some patients were hospitalized, either for a separate medical problem or to facilitate diagnostic work-up. For these patients, we still assumed the outpatient rates for the laboratory examinations done.

Cost of Therapy We attempted to quantify and calculate the cost spent by the patients for medications received and health interventions undertaken to relieve cough, all throughout the study period. We found this aspect to be the most daunting, as we encountered patients, particularly those seen at the PGH outpatient clinics, who failed to remember the names of the drugs, their dosing interval and duration of intake and needed much prompting and probing to rekindle forgotten memories, particularly for those with long-standing cough.

Table I Characteristics of patients studied

Characteristics	Completed		Lost to Follow-up		Total		p-value
	No.	%[a]	No	%[a]	No.	%[a]	
Actual No. of Patients	237	82.6	50	17.4	287	100.0	
Females	147	62.8	27	54.0	174	61.3	0.242
Age, years, mean (SD)	50.18 (18.69)		48.92 (17.76)		49.97 (18.51)		0.664
Ever smoked	57	25.0	19	44.2	76	28.2	0.010
Current smokers	15	6.6	8	18.6	23	8.5	0.016
History of atopy	35	15.1	5	12.2	40	14.7	0.629
History of prior lung Disease	55	23.7	13	28.9	68	24.5	0.529
With co-morbidities	74	31.5	14	29.2	88	31.1	0.751
Hypertension	38	16.2	9	18.8	47	16.6	0.661
Diabetes	12	5.1	5	10.4	17	6.0	0.141

[a] denominator used is number of valid responses

Our results should thus be regarded as very conservative estimates and mere baseline information for future, more formal and full economic investigations. Where records were available, these were reviewed. Clues on the identity of the drug were gathered from the mg, type of preparation, dosing interval and duration, description of the medication and its mechanism of action; for inhalers, the color and description of the inhaler and its dosing interval. When a patient could only remember what the drug was supposed to accomplish, we assumed that the drug taken was the number one-selling brand. *[IMS Health Philippines, Inc. Product Data, with permission]* These included the following: cold preparations, phenylpropanolamine/ chlorpheniramine/ paracetamol *(Neozep);* expectorants, carbocisteine *(Solmux);* antitussives, butamirate *(Sinecod);* antihistamine: cetirizine *(Virlix);* oral or inhaled bronchodilator, salbutamol *(Ventolin);* inhaled steroid, budesonide *(Budecort);* antiulcerants, ranitidine *(Zantac);* antacid, *(Kremil* S); antitubercular products, pyrazinamide/ rifampicin/ INH/ ethambutol fixed dose combination *(Myrin P);* and antibiotic, coamoxiclav *(Augmentin).*

To the patient's best recall, based on the dosing interval and actual duration of intake, we noted the actual number of tablets or bottles of medication consumed. For liquid medications, calculations were based on the number of bottles bought. If the dose, dose interval and duration of intake could not be recalled, we assumed the usual indications for the given drug and based on clinical experience, we assumed that the patient tried the medicine for a minimum of three days.

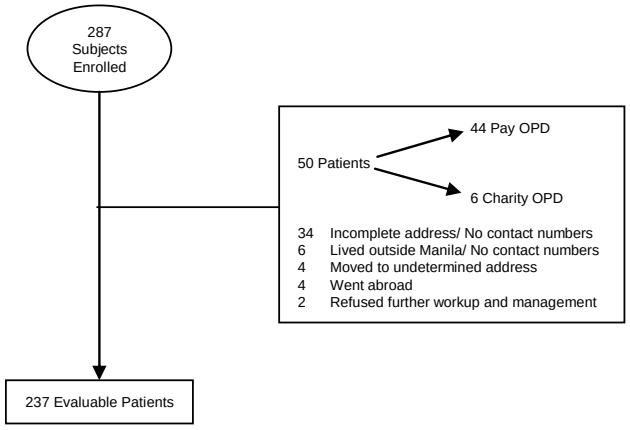

Figure 2 Patient Accounting

To standardize costing for drugs, we assumed the charges provided by the Mercury chain of drug stores, as these stores are widely distributed throughout the country and charge fixed rates.

This study did not examine consequences and thus, measurement of outcome descriptions were not made, including the benefits of withdrawal of medications or interventions. Nevertheless, such occurrences were noted and their effects on the resolution of cough were described in the other phases of the study.

Table II. Cough Description

Description	Completed		Lost to Follow-up		Total		Chi-square p- value
	No.	%	No.	%	No.	%	
Duration of cough, weeks, Mean (SD)	21.2 (52.06)		26.8 (70.64)		22.2 (55.64)		0.521[c]
Duration of cough, weeks, Mode (SD)	4.0 (52.06)		8.0 (70.64)		4.0 (55.64)		
Productive cough	139	63.8	16	59.2	155	63.3	0.647
Nocturnal cough	62	31.2	7	46.7	69	32.2	0.169[b]
Most common associated complaints	95	40.8	16	37.2	111	40.2	0.662
Dyspnea	55	23.7	10	23.3	65	23.6	0.949
Chest pain	57	24.5	6	13.6	63	22.8	0.116
Nasal symptoms	42	18.4	3	7.5	45	16.8	0.088
Post-nasal drip	101	44.1	13	31.7	114	42.2	0.139
Throat complaints	9	3.9	2	4.4	11	4.0	0.558[b]
Epigastric pain	94	40.2	20	41.7	114	40.4	0.847
Constitutional symptoms							
Recent worsening of cough	65	27.5	11	23.4	76	26.9	0.559
History of URTI prior to onset of cough	47	20.0	7	14.6	54	19.1	0.384

a denominator use is number of valid responses
b Fischer's exact test
c t-test

Table III. Cost of Consultation, Laboratory and Medicines among Immunocompetent Filipino Patients with Chronic Cough (amount in pesos)

Costing	Mean (SD)	Median	Mann-Whitney p-value	25th Percentile	75th Percentile	Range (Min - Max)
Consultation			<0.001			
Prior to first pulmo visit	330.69 (557.46)	185.00		0.00	402.94	0.00 - 5550.00
First pulmo and subsequent visits	961.04 (539.01)	897.00		492.94	1274.00	0.00 - 3675.00
Total	1291.72 (814.37)	1088.50		857.44	1570.00	0.00 - 6400.00
Laboratory			<0.001			
Prior to first pulmo visit	389.16 (1192.15)	110.00		0.00	320.00	0.00 - 12380.00
First pulmo and subsequent visits	655.11 (1096.79)	395.00		0.00	795.00	0.00 - 7510.00
Total	1044.27 (1628.02)	550.00		195.00	998.00	0.00 - 12380.00
Medicines therapy			<0.001			0.00 -
Prior to first pulmo visit	1522.60 (3896.09)	641.20		60.00	1643.25	51368.00
First pulmo and subsequent visits	2711.22 (2053.40)	2325.00		1206.15	3687.00	0.00 - 10948.50
Total	4233.82 (4756.29)	3167.75		1941.00	5033.00	0.00 - 56446.75
Total			<0.001			
Total Cost Prior to First Pulmo Visit	2242.44 (5031.66)	1062.25		345.00	2509.68	0.00 - 67538.50
Total Cost of First Pulmo and Subsequent Visits	4327.37 (2734.44)	3829.50		2274.00	5541.50	473.00 - 14923.00
Grand Total Cost	6569.81 (6099.49)	5150.00		3494.00	7940.50	473.00 - 73529.25

Table IV Total cost by etiologic diagnosis among immunocompetent Filipino patients with chronic cough

Costing	Mean (SD)	Median	p- value[a]	25th Percentile	75th Percentile	Range (Min - Max)
Total			<0.001			
Asthma	3418.32 (1352.01)	3447.50		2545.50	4415.25	678.25 - 6124.00
PNDS	3511.10 (2099.26)	2997.25		1885.50	4601.75	982.00 - 9476.95
GERD	1944.75 (1628.62)	1666.00		473.50	1628.62	473.50 - 1628.62
Bronchiectasis	4216.30 (2318.00)	4418.16		2623.44	5809.16	1216.63 - 6812.25
COPD	4706.66 (2939.58)	3502.40		2274.00	6935.50	1617.50 - 10196.50
ACEI-induced Cough	1899.81 (1188.86)	1803.00		879.88	2919.75	874.75 - 3118.50
PTB	5228.43 (2338.56)	4923.25		3946.45	5905.25	473.50 - 12642.25
Pulmonary Malignancy	5265.65 (3437.86)	3536.00		3346.50	4828.75	3304.50 - 11312.50
Post-Infectious Cough	2333.34 (1603.00)	2160.75		1498.00	2686.00	702.50 - 10084.75
Others	2210.37 (1020.57)	2080.00		1368.88	3051.87	1262.50 - 3419.00

Cost of Travel This represented costs of fare to and from the clinics for consultation, and if accomplished on a different date, for laboratory testing. We did not account for travel cost to and from pharmacies. The patients' home or office addresses were utilized for this purpose and calculations were based on the prevailing jeepney or bus fares, as applicable, at the time of consultation. At the start of the study, we attempted to calculate the cost of gasoline consumed for patients with private cars. But this proved to be tedious; consideration of car maintenance and salaries of private drivers became an enormous and impractical task. Thus, we assumed instead that all patients took the most direct and cheapest public transportation from their homes or offices to the clinics, and back. The cost of travel must be viewed as a minimum cost incurred by a patient.

Indirect Cost The cost of time lost from work represents the amount of salary that a wage-earner lost, if any, as a result of absence from work due to absences attributed to the cough, and time spent for clinic consultation and laboratory examination. This was computed at a minimum, as: Cost of Time Lost From Work (Lost Productivity) Per Day = Minimum Daily Wage x Day(s) Absent. No other indirect costs were included in the computations.

Hospital Cost Hospital costs were considered for the charity patients consulting at the PGH outpatient clinics as surrogate charges for consultation fees. These covered the cost of personal services, including physician (pulmonary fellow-in-training) cost and nursing/nurse assistant cost; and maintenance and operating cost (MOE). These were valued as follows: Physician cost = hourly wage rate of fellow x time allotted per patient Nursing cost = hourly wage rate x time allotted per patient Nurse assistant cost = hourly wage rate x time allotted per patient Maintenance and operating costs = total MOE/ total patients treated x number of study.

We assumed that each health personnel spent 15 minutes per patient. The sum of the above costs equals the hospital cost per consultation for the charity out-patients.

Table V. Cost of Consultation by Etiologic Diagnosis (amount in pesos)

Costing	Mean (SD)	Median	p value[a]	25th Percentile	75th Percentile	Range (Min - Max)
Consultation			0.03			
Asthma	773.18 (321.73)	850.00		474.00	923.00	432.00 - 1359.50
PNDS	856.72 (305.29)	895.50		532.50	920.00	459.00 - 1700.00
GERD	475.17 (4.25)	473.50		472.00	480.00	472.00 - 480.00
Bronchiectasis	968.55 (380.68)	981. 44		697.25	1239.85	497.50 - 1413.82
COPD	1043.63 (426.31)	946.00		897.00	1314.50	473.50 - 2105.50
ACEI-induced Cough	738.50 (197.22)	783.50		580.00	897.00	490.00 - 897.00
PTB	1063.97 (596.70)	886.00		524.88	1649.00	140.00 - 2362.50
Pulmonary Malignancy	1043.70 (721.04)	1050.00		532.50	1710.00	138.00 - 1788.00
Post-Infectious Cough	655.47 (232.09)	502.00		480.00	891.00	458.00 - 1275.00
Others	794.50 (408.38)	697.50		471.25	117.75	462.50 - 1320.50

[a] Kruskal-Wallis one-way ANOVA

Table VI. Cost of Laboratory Examinations by Etiologic Diagnosis (amount in pesos)

Costing	Mean (SD)	Median	p-value[a]	25th Percentile	75th Percentile	Range (Min - Max)
Laboratory			0.012			
Asthma	256.70 (375.86)	0.00		0.00	400.00	0.00 - 1385.00
PNDS	655.97 (722.06)	550.00		220.00	945.00	0.00 - 3860.00
GERD	263.33 (228.05)	395.00		0.00	395.00	0.00 - 395.00
Bronchiectasis	*787.50* (837.36)	520.00		252.50	1322.50	110.00 - 2000.00
COPD	932.07 (1294.84)	395.00		160.00	795.00	0.00 - 4000.00
ACE/-induced Cough	396.25 (324.56)	395.00		197.50	*595.00*	0.00 - 795.00
PTB	1026.17 (1535.86)	424.50		179.00	1202.50	0.00 - 7025.00
Pulmonary Malignancy	1443.10 (1889.25)	197.50		0.00	3398.00	0.00 - 3620.00
Post-Infectious cough	463.83 (1356.32)	80.00		0.00	395.00	0.00 - 7510.00
Others	465.25 (547.69)	400.00		0.00	930.50	0.00 - 1061.00

[a] Kruskal-Wallis one-way ANOVA

We did not include hospital costs for the patients who were hospitalized as this would inordinately skew the total costs and these patients were few in number.

Costs Not Considered in the Evaluation The patients were assumed to have come alone for consultation or laboratory examination and did not require home nursing assistance. Thus, we did not value costs incurred by a companion or a health assistant at home. We also did not include the cost of food since the clinic encounters are done on an outpatient basis and do not occur at crucial meal times. It is assumed that the major etiologies of chronic cough can be treated within eight weeks of consultation with a subject pulmonologist. [4] Thus, the study was limited to the monitoring of costs up to the time of resolution or significant improvement of cough (when medications were discontinued by the doctor or the patient), and in case of persistent coughers, up to two months from the time of the first visit. Maintenance medications and routine follow up visits beyond the aforementioned parameters were not valued.

Patients with health insurance benefits, whether privately obtained or provided by their employer as required by law, were noted, if these were declared. Inquiry on their annual premium and their benefit coverage was made. However, costing did not include those incurred by the health insurance companies. We also assumed that all costs were borne by the pay-patients.

Sensitivity Analysis Sensitivity analysis was performed to determine the impact of changes in certain assumptions on the study results. This was performed after the data had been analyzed. Attention was focused on those variables which contributed mainly to the entire cost, such as the cost of consultation, laboratory examination or drug therapy, including the cost of self-medication. The costs of successful and failed treatments were compared. When the data was deemed as having a wide variation with large SD's or coefficients of variation, then the percentile ranks (25^{th}, 50^{th}, and 75^{th}) were utilized instead of the 95% CI.

Statistical Analysis Data collection forms were developed and pre-tested. Data encoding was accomplished using *Epi Info* version 6.04. Statistical analyses were performed using *Epi Info* version 6.04 and *Stata 7*. Descriptive statistics such as frequencies, means ($\pm$ SD), modes, medians, ranges, and percentile ranks were obtained. The 95% CI of the means of costing data

Table VII. Cost of Medications by Etiologic Diagnosis (amount in pesos)

Costing	Mean (SD)	Median	p-value[a]	25th Percentile	75th Percentile	Range (Min - Max)
Medicines/ Therapy			<0.001			
Asthma	2388.44 (1196.65)	2475.00		1714.75	3300.00	0.00 - 5626.50
PNDS	1998.42 (1725.96)	1314.13		845.75	2931.50	0.00 - 7226.95
GERD	1206.25 (1458.89)	791.00		0.00	2827.75	0.00 - 2827.75
Bronchiectasis	2460.25 (1775.09)	2742.75		1389.50	3531.00	40.75 - 4314.75
COPD	2730.96 (1746.82)	2135.75		1377.00	4035.00	336.00 - 6027.50
ACEI-induced Cough	765.06 (835.78)	616.88		102.38	1427.75	0.00 - 1826.50
PTB	3138.29 (1343.60)	2898.50		2250.00	3764.63	0.00 - 6164.75
Pulmonary Malignancy	2778.85 (2457.61)	2772.00		1558.50	2921.25	0.00 - 6642.50
Post-Infectious Cough	1214.04 (619.30)	1124.63		835.00	1679.00	0.00 - 2589.80
Others	950.62 (726.68)	1016.38		497.63	1403.62	0.00 - 1769.74

[a] **Kruskal-Wallis one-way ANOVA**

were likewise calculated. Differences between groups were compared with *Student's t test* for two-group analyses and *ANOVA* for more than two group analyses of continuous variables, and λ^2 analysis, for categorical variables. For the costs with markedly skewed data, the Kruskal-Wallis one way ANOVA by ranks was the non-parametric procedure used. Equality of medians was measured through the Mann-Whitney-Wilcoxon rank-sum test. Sensitivity analysis for economic evaluation was likewise performed. All tests were performed at level of significance, α, $p = 0.05$

Sample Size Calculation Assuming compliance to the ACCP Anatomic Diagnostic Protocol is achieved in only 10% of patients and using the formula:

$N = [P (1-P)/CI^2] \times f (1 - £)$

N = number of patients with chronic cough to be studied

P = expected compliance rate

f (l - :£) = square of the upper ½ £ point of the standard normal distribution at 95% CI

= 3.84

CI = width of the interval

Table VIII. Cost of Consultation, Laboratory and Medicines among Filipino Patients with Chronic Cough by the Outcome of Treatment (amount in pesos)

Costing	Success			Failure			Mann-Whitney p-value
	Mean (SD)	95% Confidence Interval	Median	Mean (SD)	95% Confidence Interval	Median	
Consultation							
Prior to first pulmo visit	327.92 (564.92)	253.87, 401.97	185.00	116.67 (386.96)	127.50, 647.43	311.00	0.398
First pulmo and subsequent visits	964.70 (539.04)	894.04, 1035.36	897.00	885.78 (559.06)	510.20, 1261.36	897.00	0.620
Total	1292.62 (823.81)	1184.64, 1400.61	1,082.50	1273.24 (617.47)	858.42, 1688.06	1187.94	0.792
Laboratory							
Prior to first pulmo visit	349.42 (I141.02)	199.86, 498.99	110.00	1205.46 (1865.18)	0.0, 2458.50	160.00	0.174
First pulmo and subsequent visits	625.07 (1079.19)	483.61, 766.53	395.00	1272.36 (1321.19)	384.78, 2159.95	795.00	0.073
Total	974.50 (1596.63)	765.21, 1183.78	550.00	2477.82 (1679.94)	1349.22, 3606.42	2722.00	0.001
Medicines therapy	1518.90	997.42,	531.90	1598.71	619.63,	1077.50	0.130
Prior to first pulmo visit	(3978.31) 2682.50	2040.37 2421.93,	2,265.88	(1457.38) 3301.25	2577.80 1156.44,	2772.00	0.699
First pulmo and subsequent visits	(1987.90)	2943.07		(3192.58)	5446.05		
Total	4201.39 (4831.24)	3568.12, 4834.67	3,109.75	4899.96 (2864.57)	2975.52, 6824.40	5049.00	0.128
Total							
Total Cost Prior to First Pulmo Visit	2196.24 (5128.26)	1524.03, 2868.45	1,009.25	3191.63 (2174.72)	1730.64, 4652.63	2579.58	0.009
Total Cost of First Pulmo and Subsequent Visits	4272.25 (2667.93)	3922.56, 4621.98	3,807.00	5459.39 (3851.26)	2872.08, 8046.70	4167.25	0.421
Grand Total Cost	6468.51 (6176.96)	5658.84, 7278.19	5,073.73	8651.02 (3811.90)	6090.15, 11211.89	8723.00	0.021

Thus:

$N = [10 (100-10) / 25] \times 3.84 = 139$

Considering further a sampling design clustering effect of patients (to a specific physician) of 1.5 and multiplying this to the estimated sample size, the required number of subjects is 209. Finally, to cover for an estimated lost to follow up rate of 20%, the final minimum sample size should be 251.

Results

A total of 287 subjects were entered into the study. 262 subjects consulted at the private clinics of the study pulmonologists (91%). Twenty five patients consulted at the charity out patient clinics (9 %). Fifty patients (17% of total subjects) were lost to follow up. Six (12%) of these patients were charity patients. Thus, 24% of

Table IX. Cost of Self-Medication Prior to Pulmonary Visit (amount in pesos)

Costing	Mean (SD)	95% Confidence Interval	Median	Mann-Whitney p-value
Prior to first pulmo visit				<0.001
Doctor-prescribed	2164.23 (4647.11)	1404.09, 2924.37	1,274.75	
Self-medication	109.64 (1096.38)	320.88, 755.96	259.05	

charity and 17% of pay chronic coughers dropped out from the study.

Among the patients lost to follow up, 34 gave incomplete/wrong addresses and no/incorrect contact phone numbers; six lived outside of Manila and had no/incorrect contact phone numbers; four moved to an undetermined address; and four went abroad. Thus, the final outcome of the evaluation and treatment of cough was not known in 48 patients. The remaining two patients who were lost to follow up claimed minimal response to the initial management. Later, they preferred to take herbal medications, refusing further work up and treatment.

In all, 237 subjects remained evaluable for the economic analysis. (*Figure 2*)

Baseline Characteristics. Table I shows the baseline characteristics of all the patients entered into the study. The patients who could be evaluated were comparable to those who were lost to follow up, except for a higher rate of smokers among the latter. Majority (61.3%) of the patients were females, with mean age of 50 years. A quarter of the patients had a history of prior lung disease, usually tuberculosis while about a third of patients had other co-morbidities, the most common being hypertension and diabetes.

Table II shows a summary of the baseline cough characteristics. The mean duration of cough was 22.2 $\pm$ 55.64 weeks. Similarly, there was no difference in the cough characteristics between evaluable patients and those who were lost to follow up.

The longest duration of cough was 10 years, declared by two patients. More than 40% of subjects (41% of all subjects and 43% of the evaluated subjects) consulted for cough lasting for three to four weeks. Sixty-three percent of patients reported productive cough and about a third complained of nocturnal cough. Dyspnea, throat complaints and constitutional symptoms were common. Almost 30% of the patients noted worsening cough prior to consultation. Two out of ten patients reported symptoms consistent with an upper respiratory tract infection prior to or at the onset of cough.

Table III shows the mean total cost for consultation, laboratory examination, and drug therapy prior to the first visit to the attending physician and up to two months from the time of the first consultation. This applies only to the patients who could be evaluated. The standard deviations of the means are quite wide. Thus, the median, 25th percentile, 75th percentile and ranges of the above figures are also alternatively shown. In general, the median costs are less than the calculated mean costs.

On the average, an adult Filipino chronic cougher would spend P 6,569.81 (95% CI: 5,789.26, 7350.36) all throughout the period he/she sought relief of his/her cough. The minimum amount spent was P 473.00 and the maximum cost was P 73,529.25. The largest expenses were attributed to the few patients with chronic structural lung diseases who have spent much prior to the first visit and likewise were determined to have spent more, compared to the other patients, during the study period.

Two-thirds of this amount was found to be expenses incurred from drug therapy. As mentioned in the methodology section, the costs prior to the first visit were likely underestimated, particularly among patients with longer duration of cough, as the accounting of cost was mainly based on patient's recall. In contrast, the costs during the pulmonary consultations with the study physicians were directly determined. Each patient spent a mean P 4,327.37 (95% CI: 3,977.44, 4,677.29) during the actual study period; the minimum amount spent was P 473.00 and the maximum amount was P 14,923.00.

Among patients with a single etiology, the most expensive evaluation and management processes were demonstrated by patients who were diagnosed to have pulmonary malignancy, tuberculosis, COPD and bronchiectasis, as shown in *Table IV*.

Tables V to VII display the break down of costs per single etiology, expressed as mean (SD), 95% CI, median, 25th percentile, 75th percentile, and ranges. The higher total cost among certain etiologies of cough can be attributed to differences in the cost of consultation and medications. However, it is noteworthy in *Table VII* that among patients with asthma and postnasal drip syndrome, much of the total cost is related to drug therapy.

Further sensitivity analyses were executed to determine if the cost of treatment was influenced by the response to therapy and to attempt to measure the

cost of self-medication prior to the first pulmonary visit.

Table VIII compares the cost of treatment among the patients with treatment success or failure. It is interesting to note that the management was more expensive if the outcome failed. The higher cost among failure patients can be traced to the higher cost of laboratory examinations done and the total costs prior to the first Pulmonary visit.

A proportion of drug therapy cost was spent on self medication, although the amount varied widely from patient to patient, as shown in *Table IX*.

Only 25 patients reported absence from work due to the cough (mean days absent = 14 $\pm$ 4.77). Thus, indirect costs arising from loss of productivity were no longer included in the computation as this hardly affected the total cost.

Discussion

In our country there is limited information on the economic cost of evaluation and management of chronic cough. This study is one of a few studies that directly measured the cost of managing cough. It is the first endeavor to actually quantify how much a patient would spend while seeking relief for his/her cough.

Subject to the assumptions and limitations of costing mentioned previously, we determined that an adult Filipino chronic cougher would spend, on the average, P6,569.81 (95% CI: 5,789.26, 7,350.36) as he/she sought relief of his /her cough. Two-thirds of the amount went into drug therapy (P4,233.82). Likewise, about two-thirds of the amount was spent during the study period (P4,327.37). Although we attempted to capture all costs prior to the first visit, it is likely that these costs were still underestimated since they were based on the patient's recall, whereas the costing during the study period was more directly measured. There was wide variation in the declared costs and in general, median costs were much less than the computed mean costs, resulting in the normal curves being shifted to the right.

The most expensive individual etiologic diagnoses, as expected, were chronic and terminal diseases, including pulmonary malignancy (P5,265.65), tuberculosis (P5,228.43), COPD (P4,706.66) and bronchiectasis (P4,216.30). The higher total costs of these causes of chronic cough were related to costs of consultation (i.e., these patients consulted more frequently), laboratory tests ordered that were more expensive, and drug therapy. Bearing in mind that these costs covered only the two months of the study period, these expenses are expected to balloon further, if we take into account the cost of the maintenance phase of treatment of tuberculosis, more definitive treatment for pulmonary malignancies, and the long duration of treatment of patients with structural lung diseases.

It comes to our attention that for the two most common causes of chronic cough identified in this study, asthma and PNDS, much of the total cost was attributed to drug therapy (P2,388.44 and Pl,998.42, respectively) rather than consultation or laboratory testing. Limiting the use of non-specific cough therapy among these patients can therefore be expected to lower cost. Our study, however, did not investigate the effect of the type of drugs used per etiology on cost minimization. It would be interesting for future studies to delve into this aspect of economic evaluation. At the same time, the cost-effectiveness of empiric drug therapy versus laboratory-aided management in patients with a high suspicion of certain etiologies like asthma and PNDS should be studied in our setting.

Finally, we found in this study that failed treatments tended to be more expensive than successful treatments (P6,468.51 vs P8,65L02). This was traced to the observation that many of the former patients had terminal illnesses and underwent expensive tests like chest CT scan.

Conclusion

On the average, a Filipino immunocompetent patient will spend P 6,569.81 (95% CI: 5,789.26, 7,350.36) while seeking relief for chronic cough. Two-thirds of this amount is due to expenses incurred from drug therapy (P4,233.82). Patient will spend a mean P4,327.37 (95% CI: 3,977.44, 4,677.29) during pulmonary visits at a university teaching hospital. A failed treatment is more expensive than a successful therapy.

Limitations of the Study

The results of the study more than likely underestimated the true cost of treating cough, particularly among patients with long-standing cough of many months or years duration. For example, among patients with bronchiectasis, we did not include costs of hospitalization, vaccinations and nutritional supplements. It was also difficult to cost out herbal preparations, since these were usually homegrown (e.g., oregano, *lagundi).* Among patients with tuberculosis, the cost of the 4-month maintenance phase of the short course chemotherapy was outside the limits of the study period and was thus not considered in the computations.

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The Predictive Rule of Peak Cough Flows (PCF) on Extubation Outcome

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Background: The discontinuation or withdrawal process from mechanical ventilation is an important clinical issue. However, the conventional weaning parameters, which are very good at predicting combined outcomes, are not helpful in predicting extubation outcomes of patients who had passed spontaneous breathing trial (SBT).
Objective: To determine if cough strength, measured by voluntary cough Peak Expiratory Flow (PEF), can predict extubation outcomes of patients who passed Spontaneous Breathing Trial (SBT).
Study Design: Cross-sectional study
Methods: All patients in the Critical Care Units (CCU) who are receiving mechanical ventilatory support via endotracheal tube between January-June 2004 were examined for inclusion into the study. Patients who met the criteria being used in our Institution for possible extubation were made to undergo spontaneous breathing trial via T–piece. Patients who successfully tolerate SBT are considered for endotracheal extubation. Prior to endotracheal extubation, they were asked to cough into a peak flow meter placed in series with the endotracheal tube. The outcome measure is extubation failure or success.
Results: There were 23 patients included in the study. Cough peak expiratory flow rate measurement was done in all patients prior to endotracheal extubation. The PCF rates ranged from 60-190 L/min (mean = 121; median = 120). Extubation was successful in 17 patients. Seven subjects required reintubation within 72 hours following extubation. These patients were classified as extubation failures. Reasons of extubation failure and subsequent reintubation were inability to protect airways in four, acute hypercapnea in two, and acute myocardial infarction in one. Successful endotracheal extubation is associated with younger age, lower computed RSBI, and higher cough PEF measurements.
Conclusion: This study showed that PEF of successful extubation is higher than those who failed. Age, RSBI and PEF were however not predictive of extubation outcome. The major limitation of this study is the small sample size. *Phil Journal of Chest Diseases. Vol. 14 no. 1 pp: 40-43*

Keywords: Mechanical ventilation, weaning, spontaneous breathing trial

Introduction

The discontinuation or withdrawal process from mechanical ventilation is an important clinical issue.[1,2] The process commonly referred to as "weaning" from mechanical ventilation includes two separate steps: separation of the patient from the ventilator, and removal of artificial airway (i.e., endotracheal extubation).[3] It has been estimated that as much as 42% of the time that a medical patient spends on a mechanical ventilator is during the discontinuation process.[4] In practice, patients who tolerate carefully monitored spontaneous breathing trials are considered for endotracheal extubation. In concept, the spontaneous breathing trial (SBT) should be expected to perform well, as it is the most direct way to assess a patient's performance without ventilatory support.[5] The predictive rule of "weaning parameters" on combined liberation and extubation outcomes have been assessed in numerous studies, as well as reviewed in the 2001 Evidence-based Guidelines for weaning and discontinuing ventilatory support. The conventional weaning parameters, which are very good at predicting combined outcomes, are not helpful in predicting extubation outcomes of patients who had passed SBT. Two prospective studies[3,6] done in Bridgeport Hospital and Yale University School of Medicine, assessed the predictive value of cough strength on extubation outcomes in patients who have successfully completed SBT. In this study, we will further examine the

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Table I Cohort characteristics

N	AGE	SEX	Diagnosis	ET size	WP	DOS	RSBI	DOI	PEF	EP	EO	Cause of Failure
1	52	F	sepsis	7.5mm	T -Piece	4h	none	4d	80	clinical judgment	successful	
2	79	M	myasthenia gravis	7.0mm	T -Piece	4h	none	3d	150	clinical judgment	successful	
3	74	M	AMI	7.5mm	T -Piece	2h	97	2d	120	RSBI	successful	
4	73	M	CAP	8.0mm	SIMV/PS	24h	53	4d	can't generate	RSBI	failure	AMI
5	86	F	CAP	7.5mm	T-piece	2h	none	5d	can't generate	clinical judgment	failure	Inability to protect airway
6	86	F	CAP	7.5mm	T - piece	3h	none	6d	can't generate	clinical judgment	failure	acute hypercapnea
7	74	M	Squamous cell ca	7.5mm	SIMVIPS	4h	none	15d	can't generate	clinical judgment	failure	Inability to protect airway
8	86	F	CAP	7.5mm	SIMV/PS	5h	216	7d	150	clinical judgment	failure	acute hypercapnea
9	73	F	cerebral infarction	7.5mm	T - piece	6h	59	3d	70	RSBI	failure	Inability to protect airway
10	87	F	AMI	7.0mm	T - piece	7h	90	5d	100	RSBI	successful	
11	28	F	myasthenia gravis	7.5mm	T -piece	8h	none	4d	130	clinical judgment	failure	Inability to protect airway
12	28	F	myasthenia gravis	7.5mm	T - piece	9h	none	7d	140	clinical judgment	successful	
13	64	F	aspiration pneumonia	7.5mm	SIMV/PS	10h	62	1d	can't generate	RSBI	successful	
14	28	F	head injury	7.5mm	T - piece	11h	none	3d	120	clinical judgment	successful	
15	44	M	Esophageal Ca	8.0mm	T - piece	12h	none	2d	190	clinical judgment	successful	
16	57	M	PTB hemoptysis	7.5mm	T - piece	13h	none	2d	190	clinical judgment	successful	
17	41	F	sepsis	7.5mm	T-piece	14h	29	3d	120	RSBI	successful	
18	39	F	asthma	7.5mm	T - piece	15h	55	3d	120	RSBI	successful	
19	51	F	AMI	7.5mm	T - piece	16h	none	2d	160	clinical judgment	successful	
20	39	M	CAP	7.5mm	SIMVIPS	17h	37	11d	135	RSBI	successful	
21	69	F	CAP	8.0mm	T - piece	18h	35	3d	120	RSBI	successful	
22	66	M	COPD	7.5mm	T - piece	19h	95	4d	70	RSBI	successful	
23	81	M	asthma	7.5mm	T -piece	20h	85	2d	60	RSBI	successful	
24	23	F	GSW tempo-parietal	7.5mm	T- piece	21h	75	5d	90	RSBI	successful	

hypothesis that cough strength, measured by peak flow (in liters per minute), predicts extubation outcome.

Materials and Methods

All patients in the Critical Care Units (CCU) who are receiving mechanical ventilatory support via endotracheal tube between January-June 2004 are qualified subjects for the study. Patients are excluded if they are being extubated to comfort care (withdrawal of life-sustaining therapies, advance directive of no reintubation) or if they had a tracheostomy or they are unconscious, on sedation or cannot follow the instructions for cough peak expiratory flow rate maneuver.

Patients are assessed when they tolerate SBT and when extubation is about to be done. In our hospital, weaning is carried out by respiratory therapists, medical resident trainees and pulmonary fellows-in-training, supervised by the attending consultants. Patients receiving mechanical ventilatory support for respiratory failure generally undergo a formal assessment of discontinuation potential if the following criteria are satisfied: 1) evidence for some reversal of the underlying cause for respiratory failure; 2) adequate oxygenation (e.g. PaO_2/FiO_2 ratio > 150-200, requiring PEEP > 5 cm H_2O; FiO_2 > 40-50%; and pH > 7.30); 2) hemodynamic stability, as defined by the absence of active myocardial ischemia and the absence of clinically significant hypotension (i.e., a condition requiring no vasopressor therapy or therapy with only low-dose vasopressors such as dopamine or dobutamine, < 5 ug/kg/min; and 3) capability to initiate an inspiratory effort. It is emphasized however, that the decision to use these criteria must be individualized.

Patients who met the above criteria usually undergo spontaneous breathing trial via T-piece or pressure support $\leq$ 7 cm H_2O for 30-120 minutes. SBT is terminated if patients have respiratory distress despite

Table II Age, RSBI, PEF and extubation outcome.

	Success				Failure			
	n	range	Mean (SD)	Median	n	Range	Mean (SD)	Median
Age	17	23-87	54 (19.9)	52	7	28-86	72 (20)	74
RSBI (Breath/min/L)	10	29-97	66 (26)	68.5	3	53-216	109 (92)	59
PEF (LPM)	16	60-190	122 (38)	120	3	70-150	116 (41)	130

Table III Mann-Whitney test of age, RSBI, PEF and extubation outcome

Variable	Mann-Whitney Test result
Age	-1.910 (p=0.056)
RSBI	-0.338 (p=0.735)
PEF	0.00 (p=1.00)

attempts of bedside personnel to attenuate anxiety, increase of heart rate > 20 breaths per minute or systolic BP > 20 mmHg, respiratory rate > 35 per minute, or sustained pulse oximetry desaturations < 94% while breathing 50% oxygen. Patients who successfully tolerate SBT are considered for endotracheal extubation. Final decision to extubate, however, comes from the attending physician.

Prior to endotracheal extubation, they will be asked to cough into a peak flow meter placed in series with the endotracheal tube. Patients are positioned at 30-45° and instructed by the study personnel to perform the maneuver. Three attempts are done and the best recording is regarded as the PEF. The peak flow meter (*Airzone*, Clement Clarke Int. Ltd CM20 2TT U.K) is calibrated with a pneumotachograph using different cough flows of three healthy subjects prior to beginning the study.

The outcome measure is extubation failure or success. Patients who will not require reintubation within 72 h are classified as extubation success even if they would require reintubation later. Patients are classified as extubation failure if they would require reintubation within 72 h. Reasons for reintubation are categorized into the following: 1) hypoxemia, defined as PaO_2/FiO_2 ratio < 120 or pulse oximetry desaturations on a 100% oxygen non-rebreather facemask; 2) hypercapnea, if arterial blood analysis revealed acute hypoxemic respiratory failure (ABG showing 10% increase in pCO_2); 3) failure to maintain adequate airway for either mental status changes or inadequate expectoration; 4) AMI, hypotension/shock; and 5) others (i.e., clinician's decision).

Results

There were 23 patients who met the eligibility criteria. These patients had 24 separate extubations. There were 9 males and 15 females. Their ages ranged form 23-87 years old, with the mean age of 60. There were various causes of intubation and ICU admission. The primary reason for intubation were pneumonia in seven patients, airway protection (variety of medical conditions) in five, acute myocardial infarction in three, myasthenia gravis in three, sepsis in two, asthma in two, COPD exacerbation in one and cerebral infarction in one patient. Sizes of endotracheal tube used were 7.0mm (n-2), 7.5mm (n-19), and 8.0mm (n-3). Rapid Shallow Breathing Index (RSBI) was measured in 13 subjects and ranged from 29 to 216 breaths/minute/liter (mean = 76). Duration of intubation ranged from 24 hrs to 15 days (mean-4.4; median-3.5 days). Weaning process used was T-piece in 18 patients and Synchronized Intermittent Mandatory Ventilation (SIMV) with Pressure Support (PS) in 6 patients. All subjects tolerated SBT via T -piece modality.

The attending physicians used RSBI below 100 Breaths/Minute/Liter as endotracheal extubation parameter in 12 subjects. One subject though was extubated even if the computed RSBI is 216. Patients who were successfully extubated (n = 10) had lower computed mean RSBI than those patients (n = 3) who failed (66 vs 109).

No particular extubation parameter was used for the other 12 patients. In these patients the attending physicians made use of their clinical judgment in their decision to liberate patients from endotracheal tube.

Cough peak expiratory flow rate measurement was done in all patients prior to endotracheal extubation. The PCF rates ranged from 60-190 L/min (mean = 121; median = 120). Five patients were not able to generate flow rates. Four of whom required reintubation within 72 hours. The other one had successful endotracheal extubation.

Endotracheal tube was taken out as per instruction of the attending physician.

Extubation was successful in 17 patients. Seven subjects required reintubation within 72 hours following extubation. These patients were classified as extubation failures. Reasons of extubation failure and subsequent reintubation were inability to protect airways in four, acute hypercapnea in two, and acute myocardial infarction in one.

Successful endotracheal extubation is associated with younger age, lower computed RSBI, and higher cough PEF measurements (*Table II*)

Mann-Whitney test showed that age, RSBI, and cough PEF were not predictive of extubation outcome (*Table III*).

Discussion

This study showed that cough PEF of patients who were successfully extubated is higher than those who failed extubation. The finding of an association between cough strength and extubation outcomes is not new.[6,7] In the previous study,[6] cough strength was assessed semi-objectively using a white card placed 1 to 2 cm from the open end of the endotracheal tube and subjectively on a 6-point scale. Using peak flow meter connected in series at the open end of the endotracheal tube, provides a more objective and reproducible measurement of cough strength. Bach and Saporito[8] examined the effects of cough peak flows on extubation outcomes. The study involved 49 tracheotomized patients with chronic respiratory failure due to neuromuscular disease. They found out that cough PEFs were greater in those who were successfully decannulated, and that flow rates of 160ml following decannulation demarcated successes from failures. However, the method used to elicit PEFs was different: patients coughed from a maximal insufflation with a manual assist. Our study consisted of a general medical population of critically ill patients, involving three patients with neuromuscular disease. Moreover, peak flows through an endotracheal tube are bound to be lower than those in decannulated patients because intubated patients cannot close their glottis, thereby limiting the pressure generated when one attempts to cough. The patients in our study performed a "glottic-free PEF."

This study is limited by the small population size. And by the fact that voluntary cough PEF is effort dependent.

Conclusion

PEF of successful extubation is higher than those who failed. Age, RSBI and PEF were not predictive of extubation outcome.

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Outcome of Non-invasive Ventilation on Unplanned Extubation in the Adult Intensive Care Unit

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Most patients who fail to tolerate unplanned extubation had been receiving full ventilatory support. Rapid reinstitution of ventilatory support and control of the airway of these patients may prevent the development or reduce the severity of complications. The act of re-intubation however is not without complications. To examine the impact of non-invasive ventilation (NIV) on unplanned extubation on hospital outcome, we performed an analysis of prospectively gathered data in a tertiary-care intensive care unit (ICU). We followed 240 ventilated patients over a nine-month period. Thirty-nine (16%) episodes of unplanned extubation were recorded. Nine (4%) episodes were excluded (four were hemodynamically unstable, three had unplanned extubation during a weaning trial, and two received oxygen therapy alone). Thirty (12.5%) occurred during full ventilatory support and were included (15 received NIV, 15 received IMV). Both groups were matched for age, sex, and presence of co-morbid conditions, indications for mechanical ventilation and Acute Physiologic and Chronic Health Evaluation II score. In-hospital mortality was similar in both groups (NIV 27%, versus IMV 40%, *p=0.698*). Patients who received NIV had a significantly shorted duration of ventilatory support (five versus 11d, *p<0.05*) and shorter stay in the ICU (12 versus 17d, *p<0.05*). There was no difference in overall hospital stay. Complications such as pneumonia were less common among the NIV group (3 versus 9) but this did not reach statistical significance (*p=0.064*). This study indicated that unplanned extubation during full ventilatory support can be successfully managed with noninvasive ventilation, providing measurable benefits on reduction of the duration of total ventilatory days and ICU stay. *Phil Journal of Chest Diseases. Vol 14 No. 2 pp: 44-52*

Keywords: Mechanical ventilation, weaning, non-invasive ventilation

Introduction

Unplanned extubation is a major complication of trans laryngeal intubation, occurring in 3-16% of mechanically ventilated patients.[1] Successfully managed unplanned extubation has the potential of improving outcome by shortening the duration of intubation,[2] thereby reducing the patient's exposure to the complications of mechanical ventilation. Rapid reinstitution of ventilatory support and control of the airway of these patients may prevent the development or reduce the severity of complications. Reintubation, however, carries an increased risk for morbidity and mortality. The role of Noninvasive Positive Pressure Ventilation (NPPV) in the management of acute respiratory failure secondary to congestive heart failure and exacerbations of chronic obstructive pulmonary disease has been well established. The clinical efficacy of Noninvasive Positive in the management of respiratory failure, especially acute-on-chronic[3,4] respiratory failure, has been demonstrated to be of value. It also have value in the management of persistent weaning failures and likewise for patients with pneumonia.[6] Studies[7,8] have suggested that the benefit of NPPV may be extended to the prevention and managing respiratory failure after extubation. NPPV has been shown to decrease the need for reintubation and the duration of mechanical ventilation[7]. However, the efficacy of NPPV has not been assessed by randomized controlled trials in preventing the development of respiratory failure after a patient tolerates a spontaneous breathing trial, nor in preventing reintubation after post-extubation respiratory failure[9]. NPPV as a supportive measure after unplanned extubation is viewed to be of benefit in reducing complications arising from such an event

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and in improving outcomes in selected patients. No prospective data are available to assess the efficacy of noninvasive ventilation in preventing reintubation after an episode of unplanned extubation.

We therefore undertook this study to determine the outcome of Non Invasive Ventilation in patients who had an unplanned extubation.

Methodology

Setting: Intensive Care Units of the Philippine Heart Center, namely the Medical, Surgical, Coronary and Neurology ICUs with a combined 60-bed capacity.

Definition of Terms: *Non Invasive Ventilation or Noninvasive Positive Pressure Ventilation (NIV or NPPV).* Administration of positive pressure ventilation through face mask or nasal mask. *Planned Extubation.* Extubation occurring after the patient has tolerated a Spontaneous Breathing Trial (SBT) for 30 minutes to two (2) hours *Unplanned Extubation (UEX).* Extubation unwanted by the medical staff, which may either be: a) deliberate removal of the endotracheal tube by the patient; or b) accidental removal of the endotracheal tube

Criteria for weaning from mechanical ventilation. Arterial Oxygen Tension > 60 mm Hg with FiO_2 < 0.4; alert mental status; stable hemodynamic status (BP > 90/60 mm Hg); Maximal Inspiratory Force > 15 cm H_2O; Compliance (Static and Dynamic) > 30 cm H_2O; Rapid Shallow Breathing Index < 10

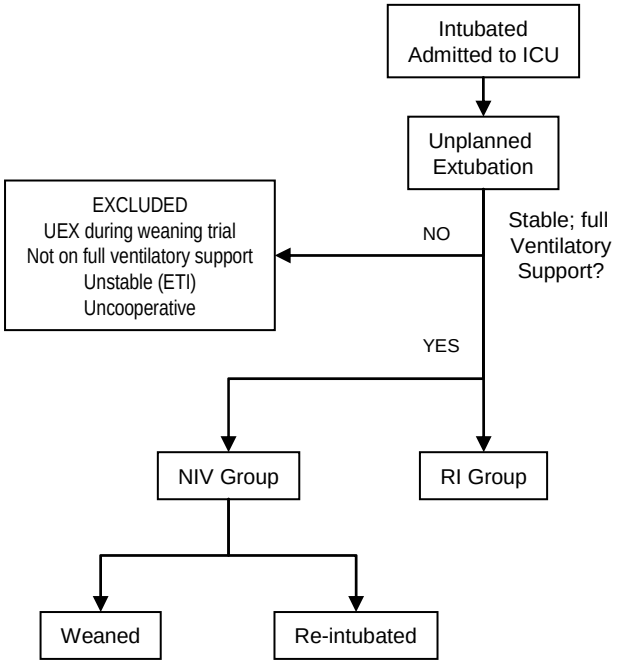

Figure 1 Schema of study methodology

Selection Criteria for NIV (2/3 *criteria). Moderate* to severe dyspnea with use of accessory muscles and paradoxical abdominal motion; moderate to severe acidosis (pH 7.30-7.35) and hypercapnea (pCO_2 = 45 - 60 mm Hg); respiratory rate > 25 per minute

Exclusion criteria for NIV (any may be present). Respiratory arrest; cardiovascular instability; somnolence, impaired mental status, uncooperative patient; high aspiration risk; viscous or copious secretions; recent facial or gastroesophageal surgery; craniofacial trauma, fixed nasopharyngeal abnormalities; extreme obesity

Criteria for reintubation (after failure of NIV). Increase in $PaCO_2$ > 10 mm Hg; decrease in pH > 0.10; PaO_2 < 60 mm Hg; SaO_2 < 90% on FiO_2 > 0.50 to 1.0; inability to protect the airway because of upper airway obstruction or excessive pulmonary secretions.

Study Design: Prospective, cohort

Patient Selection. *Inclusion*: All patients 19 years old and above, who are intubated and on full ventilator support and admitted at the Medical, Surgical, Coronary and Neurology ICU units of the who had an unplanned extubation.

Group I: Patients receiving Non Invasive Ventilation after an episode of unplanned extubation (UEX-NIV)

Group II: Patients receiving Invasive mechanical ventilation after an episode of unplanned extubation, (UEX-RI)

Exclusion: Patients who had an unplanned extubation that occurred at the time of weaning were excluded. Those who were hemodynamically unstable, suffered from cardiac arrest or cardiac arrhythmia at the time of unplanned extubation who require immediate endotracheal intubation (labeled as ETI) were likewise excluded. Patients who would not give an informed consent and who are uncooperative were also excluded. Extubation for the purpose of replacing a defective endotracheal tube were not included.

All patients included were followed prospectively until discharged from the ICU and from the hospital, or until death. Primary endpoints: need for mechanical ventilation. Secondary endpoints: survival, frequency of complications, duration of ventilatory support

Table I. Demographic and Clinical Characteristics of the Patients at entry into the Study

Characteristics	UEX-NIV (n=15)	UEX - RI (n=15)	P value
Age, years	62 ± 11	60 ± 10	0.647
Sex Ratio, M/F	11/4	6/9	0.698
APACHE II Score	14.6 ± 4.48	14.6 ± 2.99	1.000
Co-morbid conditions, n			
Hypertension	11	11	1.000
Coronary Artery Disease	12	15	0.224
COPD	5	3	0.681
Diabetes mellitus	6	5	1.000
CVD history	2	0	0.482
PVOD	1	0	1.000
RHD, MS	0	3	0.223
Community Acquired Pneumonia	3	3	1.000
Acute Coronary Syndrome	8	7	1.000
Chronic renal Failure	2	3	1.000
Causes of Intubation, n			
Pulmonary edema	12	15	0.224
Pneumonia	1	0	1.000
COPD exacerbation	2	0	0.482
Previous episode of MV, n	3	1	0.597

UEX-NIV: Unplanned Extubations followed by NIV
UEX-RI: Unplanned Extubations followed by reintubation

Table II. Physiologic parameters of patients at entry into the study

Parameters	UEX-NIV	UEX-RI	p value
RR, bpm	28 ± 9	27 ± 7	0.806
Heart rate, min.	114 ± 16	105 ± 21	0.199
Mean BP, mm Hg	80 ± 22	71 ± 10	0.171
Hematocrit, L/L	37 ± 7.30	36.8±7.10	0.860
White Blood Cells, x 10^9/L	16.8 ± 3.92	14±4.17	0.059
Arterial pH, mm Hg	7.41 ± 1.06	7.41 ± 0.46	0.947
$PaCO_2$, mm Hg	39.2 ± 12.83	36.1 ±6.41	0.404
PaO_2, mm Hg	138.6 ± 67.5	126 ± 42.5	0.556
PaO_2/FiO_2	255.8 ± 139.03	246.1 ± 113.3	0.835
Temperature, °C	36.5 ± 0.52	36.7 ± 0.54	0.270
Sodium, mmol/L	139 ± 5.9	137.6 ± 8.5	0.606
Potassium, mmol/L	4.11 ± 0.45	4.25 ± 0.52	0.439
Creatinine, mgl dL	1.75 ± 0.87	1.95 ± 1.57	0.670

UEX-NIV: Unplanned Extubations followed by NIV
UEX-RI: Unplanned Extubations followed by reintubation

(invasive MV, NIV), duration of ICU stay, and duration of hospital stay.

Procedure. All 240 patients mechanically ventilated and admitted to the ICU complex of the St. Luke's Medical Center over a nine-month period were prospectively followed. Patient to nursing staff ratio was 1:2 to 1:3. Cloth tapes were used to secure all endotracheal tubes in place. Clinical, physiologic, and laboratory data were collected from all patients six hours after the onset of mechanical intubation. Acute Physiologic and Chronic Health Evaluation (APACHE) II scores were likewise determined during the first six hours of intubation. Mechanical Ventilators used were: *Puritan Bennett 7200, NMS Breeze, Newport Wave, Gallileo (Hamilton Medical), Gallileo Gold (Hamilton Medical),* and *Raphael (Hamilton Medical).*

They received an initial MV setup of 1.0 FiO_2, tidal volumes were set at 6-8 mL/ kg, frequency was set four breaths below the inherent respiratory rate, and a 5 cms H_2O PEEP for atelectasis prevention. Subsequent modifications in the MV setup depended on adequacy of oxygenation and general clinical condition. Patients were assessed on the first hour of unplanned extubation as to eligibility for entry into the study.

About 39 patients (16%) had unplanned extubation. Among these, 30 (12.5%) occurred during full ventilatory support ($FiO_2 \geq 0.5$, PEEP $\geq$ 5 cms H_2O) and were included. Selection and exclusion criteria were predefined. Among the nine patients who were excluded, four were hemodynamically unstable and did not meet the selection criteria were immediately re-intubated, three had unplanned extubation episodes during a weaning trial, and two patients were uncooperative and were given oxygen therapy thru face mask alone.

Patients eligible for entry into the study were randomized into two groups. Group I (UEX-NIV) received Non Invasive Ventilation and group II (UEX-RI) received invasive mechanical ventilation. A critical care ventilator in BiPAP mode (*Gallileo, Hamilton Medical*) was used for the institution of Non-Invasive Ventilation delivered thru a face mask. The proper mask size was chosen for each patient. A nasal mask was optionally used if patients did not tolerate the facemask. After the mask was secured, initial levels were set.

The level of pressure support (PS) was set at 8 cm H_2O, and increased by 2 cms H_2O at a time to reduce $PaCO_2$, reduce dyspnea, and use of accessory muscles. An initial PEEP of 5 cm H_2O was applied, and increased by 2 cm H_2O at a time to increase PaO_2. PS and/or PEEP were adjusted if ventilator efficiency was thought to be insufficient. The maximum PS (and PEEP) was 20 cm H_2O. Arterial blood gases were measured after 30 min of initiation of ventilation. The

Table III. Comparison of outcomes

Outcomes	UEX-NIV	UEX-RI	p value
Mortality, n	4	6	0.698
Survivors, n	11	9	
Timing of deaths During NIV / RI period After NIV / RI period	 0 4	 5 1	 0.042* 0.0615
MV days, d	3.57 ± 3.16	4.10 ± 3.76	0.677
Total days of ventilatory support, d	4.93 ± 3.38	11.44 ± 6.73	0.002*
ICU days, d	12.2 ± 5.77	17.13 ± 6.83	0.041 *
Hospital days, d	19.8 ± 9.46	25.66 ± 12.16	0.156
Tracheotomy, n	1	0	1.000
Causes of Death after entry into the study Multi-organ failure, n Sepsis, n Congestive Heart Failure, n Arrhythmia, n	 2 2 1 1	 5 5 1 1	 0.389 0.389 1.000 1.000

UEX-NIV: Unplanned Extubation followed by NIV
UEX-RI: Unplanned Extubation followed by reintubation
MV days: duration of mechanical ventilation prior to unplanned extubation; Total days of ventilatory support: duration of invasive mechanical ventilation prior to unplanned extubation plus duration of either Non Invasive Ventilation or mechanical ventilation after reintubation.
* statistically significant

Table IV. Serious complications diagnosed in the ICU after entry into the Study

Complications	UEX-NIV	UEX-RI	p value
Nosocomial pneumonia/ VAP, n	3	9	0.064
Decubitus ulcer, n	0	2	0.482
UTI,n	2	0	0.482
GI Bleeding, n	1	2	1.000
Septic Shock, n	1	2	1.000
Acute renal failure	4	2	0.651

UEX-NIV: Unplanned Extubation followed by NIV
UEX-RI: Unplanned Extubation followed by reintubation

Table V. Causes of unplanned extubation

Causes	UEX-NIV, n	UEX-RI, n	TOTAL
Deliberate	15	15	30
Air leak in tube cuff	0	0	0
Inadequate fixation	4	7	11
During nursing procedure	0	0	0
During transport	0	0	0
Lack of sedation when needed	6	10	16

FiO_2 was adjusted to maintain SaO_2 ~ 90% as measured by a bedside pulse oximeter.

NIV was continued for at least the first 24 hours after the unplanned extubation, except when indications for invasive ventilation were observed. Criteria for reintubation during this period were predefined. Group II (UEX-RI) receiving invasive mechanical ventilation were reconnected to their ventilators with ventilatory adjustments made to maintain $SaO_2 > 90\%$. Subsequent adjustments depended on adequacy of oxygenation and clinical condition.

Statistical Analysis. Quantitative variables are expressed as mean ± SD and were compared through the Student's *t test*. Qualitative variables are expressed as percentages and were compared through the chi square method with a two-tailed Fisher's exact test. A $p < 0.05$ was considered significant.

Results

Patient Demographics and Physiologic Parameters. The demographic and clinical characteristics of subjects are shown in *Table I*. The 30 patients consisted of 17 men and 13 women with a mean age of 61 ± 1 year. Fifteen were randomized into the NIV group, while the same number was randomized into the Re-intubated group. The patients in both groups were well matched with regard to age and sex and underlying co-morbid conditions. The APACHE II scores 14.6 ± 4.48 and 14.6 ± 2.99 for the NIV and Re-intubated groups respectively, which showed no significant difference. Causes of intubation were likewise well matched, as with previous episodes of endotracheal intubation.

At the time of inclusion, physiologic parameters and laboratory data were determined in both groups (*Table II*). There was no significant difference in the breathing pattern, blood pressure and arterial blood gas values in both groups. Likewise, no significant difference was seen in temperature, serum Sodium, Potassium and Creatinine values in both groups.

Comparison of Outcomes. Outcomes in the 15 patients treated with NIV and 15 patients treated with reintubation after an episode of unplanned extubation are shown in *Table III*. In-hospital mortality was not significantly different in the NIV group versus the Reintubated group (4% versus 6%). When the timing of deaths was considered, no patients in the NIV group died during the NIV period. Five patients, however died in the Reintubated group during the time of invasive mechanical ventilation. Duration of mechanical ventilation prior to the episode of unplanned extubation was not significant in both groups. Patients who were intubated after, however, required a longer duration of mechanical ventilation after reintubation (4.93 ± 3.38 versus 11.44 ± 6.73, $p = 0.002$). There was no significant difference, however, when total hospital stay was considered.

Causes of death after entry into the study showed no difference in the incidence of multi organ failure, sepsis, congestive heart failure and fatal arrhythmias. Among the NIV group, two required reintubation due to progression of pulmonary edema (1) and development of pneumonia (1).

Complications Diagnosed after Entry into the Study. Complications diagnosed at the Intensive Care Unit after entry into the study are shown in *Table IV*. There was a trend towards a lower incidence of complications in the UEX-NIV group. However, these differences did not reach statistical significance. Among patients who received Non-Invasive Ventilation, three had pressure ulcers related to wearing a ful1-face mask.

Causes of Unplanned Extubation. Causes of episodes of unplanned extubation in both groups are shown in *Table V*. Deliberate removal of the endotracheal tube occurred in al1 patients. Inadequate fixation and lack of sedation accounted for the rest of the causes of unplanned extubation.

Analysis of Survival. Survival compared with patients treated with NIV and Reintubation after unplanned extubation showed no significant difference. The causes of death within 60 days of randomization are summarized in *Table III*.

Discussion

Providing mechanical ventilation in critically ill patients remains an effective means of managing various forms of respiratory failure. Withdrawal of mechanical ventilation becomes a primary goal after resolution or significant improvement of the underlying indication for mechanical ventilatory support. Majority of these patients require gradual withdrawal of ventilatory support through weaning. The process of discontinuation of a mechanical ventilatory support may be a major challenge in a number of patients, especially those with chronic airflow obstruction and persistent weaning failure. Managing unplanned extubation in patients receiving full ventilatory support and whose underlying indications for ventilatory support are not fully resolved, thus becomes a concern. This study focuses on the efficacy of noninvasive ventilation as a supportive measure in providing ventilatory support in these patients.

The role of noninvasive ventilation in the management of various forms of respiratory failure has been the subject of numerous studies. In recent years, noninvasive ventilation has been used increasingly to avoid endotracheal intubation and its attendant complications in patients with acute respiratory failure.[11] The role of noninvasive ventilation has been well established in the management of acute exacerbations of chronic obstructive pulmonary disease.[7,11] For the management of cardiogenic pulmonary edema, the evidence remains to be stronger for the use of CPAP than for NPPV although the latter may theoretically be more effective than the former because a greater reduction in the work of breathing and a more rapid alleviation of hypercapnea and dyspnea might be superimposed on the benefits achieved with CPAP.[7,12]

The success of NPPV depends not only on the proper institution of NPPV but on the selection of appropriate clinical conditions or settings as well. Several determinants of success for NPPV in the acute setting especially among patients with chronic airflow obstruction, has been identified: synchronous breathing, intact dentition, low APACHE scores, less air leaks and secretions,[13] good initial response to NPPV (correction of pH, reduction in respiratory rate and $PaCO_2$)[14] and no pneumonia.[13,15] Recent studies[6,18] on the application of NPPV in patients with pneumonia however, show conflicting results. A randomized trial[18] of NPPV among patients with pneumonia without COPD showed initial improvements in oxygenation and respiratory rates after initiation of NPPV. However, 66% eventually required intubation. The benefit of NPPV in this case has not been well established due to the lack of controlled trials. These conditions should be considered in trying to establish a successful ventilatory management, while avoiding conditions where NPPV is most likely to fail (exclusion criteria for NIV).

Noninvasive ventilation has likewise been employed as a means of managing post-extubation respiratory failure. Extubation failure occurs in 5 - 20% of planned extubations[13] and 40 - 50% of unplanned extubations.[16] Mortality rates in extubation failure were considerably higher than in those patients who succeed after extubation (42% versus 12% respectively).

It was estimated that reintubation after post-extubation failure figured at 15 - 20% of patients extubated after a successful spontaneous breathing trial. Reintubation occurred within 48 - 72 hours after extubation. Several studies have investigated the

efficacy of noninvasive ventilation in avoiding reintubation after extubation failure. However, no randomized controlled trials have been published assessing the efficacy of noninvasive ventilation in preventing the development of post-extubation respiratory failure in this scenario. Noteworthy is the overwhelming evidence (Level I) that intubation and reintubation should be avoided, if possible, as it increases the risk for ventilator-associated pneumonia (VAP).[19] The use of noninvasive ventilation is likewise recommended (Level I) whenever possible in selected patients with respiratory failure.

With the expanding boundaries for the use of noninvasive ventilation, management of unplanned extubation remains a potential field of application for noninvasive ventilation. Unplanned extubation remains to be a major complication of trans-laryngeal intubation, and poses significant life-threatening complications and risks for pneumonia and additional length of mechanical ventilation as described by some authors. Several studies[1,2] have reported unplanned extubation to occur in 3-16% of mechanically ventilated patients. This is comparable to the rate of unplanned extubation at 16% observed in our study.

As a means of managing extubation failure, Jiang[8] examined the effect of BiPAP on the outcome of extubation by enrolling 93 extubated patients, 56 after planned and 37 after unplanned extubation. In this study, 28% of patients randomized to receiving NPPV required reintubation compared to only 15% in control subjects who received unassisted oxygen therapy. The authors noted no correlation between extubation outcome and post-extubation respiratory management, whether BiPAP or unassisted oxygen therapy. It was further concluded that early application of BiPAP did not predict a favorable extubation outcome, and did not support the "indiscriminate" use of NPPV in avoiding post-extubation failure. The study however, had problems with randomization in that more patients who had an episode of unplanned extubation were assigned to receiving NPPV, with most failures coming from these patients. There are presently no prospective data available to assess the efficacy of noninvasive ventilation in preventing reintubation in this clinical situation. Although there is a paucity of adequate controlled trials to support the use of NPPV in avoiding reintubation after extubation failure, the use of NPPV is deemed justifiable in carefully selected patients.

In this study, we employed the use of noninvasive ventilation (NPPV) as a means of managing unplanned extubation whose causes of intubation were varied, with most of the cases due to cardiogenic pulmonary edema (90%), and the rest being exacerbations of chronic airflow obstruction (6%) and pneumonia (4%). There was no significant difference between the two groups (see table 1). Although the evidence for the use of CPAP is stronger than NPPV in cardiogenic pulmonary edema, the act of unplanned extubation extols on the patient much effort to breathe harder and increase the work of breathing after the event, and it is viewed that it is in this scenario that NPPV can best work. Furthermore, our study employed noninvasive ventilation among those patients who are receiving full ventilatory support at the time of unplanned extubation - a clinical scenario that points to the fact that these patients may yet require some form of ventilatory support that an NPPV may provide. Unplanned extubation that occurred in patients undergoing weaning, or those that do no longer receive full ventilatory support were not included in this study as these patients may actually tolerate unassisted oxygen therapy.

While the use of noninvasive mechanical ventilation reduced the complications of prolonged mechanical ventilation and mortality in some studies,[4-6] concerns has been raised on the safety on NPPV, especially among patients with acute myocardial ischemia or infarction. Mehta and coworkers[20] compared the outcome of CPAP to NPPV in the treatment of patients with acute pulmonary edema. This study showed that BiPAP improved ventilation and vital signs more rapidly than CPAP. Dyspnea scores, respiratory and cardiac frequency, $PaCO_2$ and pH were significantly improved in the BiPAP group. In patients who received CPAP, only respiratory rate improved from baseline. This study showed a greater rate of myocardial infarction in the NPPV group and the study was stopped after enrolling 27 patients. This study however, was critiqued to have unequal randomization with more patients with chest pain randomized in the NPPV group. Levitt,[21] on the other hand, showed no difference in the myocardial infarction rate among patients managed with NPPV to high-flow oxygen by mask through a randomized controlled trial. A prospective randomized-controlled trial in 40 patients by Masip and coworkers[22] further compared noninvasive ventilation with unassisted oxygen therapy in addition to standard medical therapy. This

study showed a reduction of the rate of intubation and a more rapid resolution of the abnormal physiology among the NIV group. It was further noted that about 33% of patients who received unassisted oxygen therapy required intubation, in contrast to only 5% in those receiving NIV. The time to reduce respiratory rates and improvement of oxygen saturation was likewise shorter in the NIV group. This study however, found no difference in survival or hospital length of stay. As there are no large studies comparing CPAP and NIV, it is therefore recommended[11] that NPPV be considered if patients continue having hypercapnea and unimproved dyspnea after CPAP institution, pending further studies. Moreover, suggested absolute contraindications to the application of noninvasive ventilation like coma, confusion, inability to protect airways and hemodynamic instability (including acute myocardial infarction) have been set, which the clinician must identify prior to employing the use of noninvasive ventilation. However, these contraindications have been determined as these were exclusion criteria for various controlled trials; hence the use of noninvasive ventilation in these circumstances is not proven.

In this study, 27 patients (90%) had diagnosed cases of coronary artery disease with 15 (50%) of subjects admitted due to acute coronary syndromes (see *Table I*). We have observed no extension of myocardial infarction, or the occurrence of new myocardial events among those eight (27%) patients randomized into the NIV group.

Complications most frequently encountered in the institution of NPPV are related to the mask (namely nasal bridge erythema or ulceration, or mucosal pain) and ventilator airflow pressure (pneumothorax).[23,24] Others include gastric insufflation, eye irritation, nasal congestion, mucosal dryness and claustrophobia.[25] None of these were observed among the patients in this study.

Likewise, we have demonstrated a reduction in the total days of ventilatory support with the use of NPPV after an event of unplanned extubation. Clinical improvements were seen in these subjects as reflected through a reduction in the days of stay at the intensive care, where we have demonstrated a significant reduction in this group. This can eventually be correlated to a reduction in the risk of ventilator-associated complications such as ventilator associated pneumonia (VAP), and more meaningfully a reduction in the cost of hospitalization in a practical sense. No data from large randomized studies is yet available showing a reduction of these risks and complications. We likewise observed no difference in the total duration in hospital stay. This may be attributed to the fact that some patients may have not been able be discharged because of some other medical problems yet to be controlled, or more importantly because of financial constraints as expenses during the admission to the intensive care and succeeding days of continued medical care may have mounted.

In this study, we have not demonstrated a reduction in the occurrence of ventilator-associated pneumonia between the two groups; however, a trend towards a lower occurrence of nosocomial pneumonia was observed in the NIV group. A larger sample size may better evaluate this area. The over-all in-hospital mortality was not significantly different between the two groups; however, it is noteworthy that no deaths occurred during the institution of noninvasive mechanical ventilation. The four (13%) mortalities recorded in this group occurred after patients have been weaned from NPPV (see *Table III*). In comparison, out of the six (20%) mortalities recorded among the re-intubated group, five (17%) required prolonged intubation. These patients continued to deteriorate clinically, and developed sepsis. These data shows that much of the patients who had episodes of unplanned extubation still require ventilatory support, especially those whose reasons for intubation had not been fully resolved, and are currently receiving full ventilatory support.

Various studies have enumerated predictors of unplanned extubation. One study[6] showed that 50-78% of these airway accidents may either be completely or partly preventable. It is in this sense that focus must be given with respect to adequate nurse staffing and supervision, an adequately secured endotracheal tube, sedation when deemed necessary and appropriate early weaning.

We have noted a 1:3 nurse-to-patient ratio in the intensive care unit where most of the episodes of unplanned extubation occurred. A 1:1 or 1:2 ratio had been recommended to be more acceptable. The finding that all of the subjects had deliberately self-extubated stresses the need for a more adequately staffed unit. Most of the subjects (53%) were assessed to require adequate sedation. A sedation protocol may have significantly reduced this occurrence.

It is important to note that while management of unplanned extubation may be managed effectively by noninvasive ventilation, it is likewise imperative to

stress that unplanned extubation are an unwelcome occurrence in the intensive care unit. Vigilance in detecting patients who are at risk of self-extubation is in order in any clinical setting. Maintaining adequate staffing in the intensive care unit has likewise been shown to reduce patient's length of stay, improve infection control practices, and reduce duration of mechanical ventilation.[19] Reducing occurrence of unplanned extubation that may be related to reduction of the duration of intubation and mechanical ventilation can be achieved and thus reduce complications such as ventilator-associated pneumonia with the use of sedation protocols. It is viewed that most unplanned extubation would not have happened if patients had been sedated while on mechanical ventilation.

Reduction in the duration of stay in the intensive care unit and hospital stay may have important economic implications and are important factors to consider when faced with a critically ill patient in the intensive care with respiratory distress after an unplanned extubation. Immediate institution of ventilatory support is essential, especially in patients who received full mechanical ventilatory support and whose underlying abnormal physiologies are yet to be corrected. Invasive mechanical ventilation is an important tool as a life-saving procedure, but reintubation with its attendant risks, is inherent as with risks of prolonged mechanical ventilation, ICU and hospital stay, and risks of hospital acquired infections. Mortality increases with the duration or time between extubation and reintubation.[27] Hence, the decision to re-intubate or apply other means of ventilatory support should be in mind in the face of unplanned extubation. Noninvasive ventilation provides adequate ventilatory support in various cases of respiratory failure. Studies on the use on noninvasive ventilation to avoid mechanical ventilation have been well-documented, with the greatest evidence among patients with chronic airflow obstruction. Its role in the management of post-extubation respiratory failure, whether planned or unplanned is an expanding field for its application. To date, there are no large trials comparing invasive mechanical ventilation, noninvasive mechanical ventilation and unassisted oxygen therapy in the management of unplanned extubation.

Limitations

This study is limited by the relatively small sample size and could lead to wide variations in values that may not be reflective of the larger, general population of critically ill patients receiving mechanical ventilation. A larger sample size will enable us to do multiple regression analysis. We were likewise not able to demonstrate the improvement in oxygenation upon institution of noninvasive ventilation in comparison to values immediately after the event of unplanned extubation. Further studies in this area may be assessed in future undertakings.

Conclusion

This study indicated, despite its limitations, that unplanned extubation during full ventilatory support can be successfully managed with noninvasive ventilation, providing measurable benefits on reduction of the duration of total ventilatory days and ICU stay.

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The Use of Arm Span Measurement as Surrogate for Measured Standing Height in the Prediction of Lung Volumes among Filipinos.

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Background: Pulmonary function testing is an important part in the evaluation of many patients referred to the pulmonary department. Comparing the patient's actual performance to predicted values forms the basis of this evaluation. The age, sex, race and standing height are the variables most frequently used to develop reference values in pulmonary fimction. Of all the physical parameters that can be measured in the human body, lung function best correlates with actual standing height. In circumstances were measuring the actual standing height is difficult and inaccurate the use of arm span measurement has been proposed as a surrogate for standing height.

Objectives: To determine whether arm span measurements can be used as a surrogate for measured standing height in the prediction of lung volumes among Filipino patients.

Methods: This is a prospective, cross sectional study using arm span measurement in the prediction of lung volumes and comparing these with the results of the spirometric test when actual measured standing height was used. Included in the study were individuals 18 yrs old and above referred to the department for spirometric test. Excluded from the study were subjects in whom height can not be measured correctly due to presence of structural defects of the spine, and those with upper limb deformities in which arm span can not be measured accurately. Arm span was measured using a flexible steel tape from the tip of the middle finger of one hand to tip of the middle finger of the other hand of maximally outstretched arms with the subject back facing the wall. Height was measured using the standard stadiometer in centimeters.

Results: A total of 459 subjects were entered into the study, 252 (55%) were males and 207 (45%) were females, the youngest was 19 years old and the oldest was 90 years old. Measured height ranges 120-183 cms with a mean of 157.97 SD 9.57, arm span measurement was slightly higher ranges 120-190 cms with a mean of 158.12 SD 9.77. A direct correlation was seen between measured standing height and arm span with a correlation co-efficient r=0.794 p value= 0.000 (2 tailed). There was also direct correlation between the predicted lung volumes, 0.911 for FEV_1 and 0.915 for FVC. Absolute Difference (*t-test* for the equality of means) of correlations between actual measured height and the lung volumes shows that the mean difference between the two variables 11.80 for height and 11.63 for arm span was not statistically significant. For Estimates of Agreement when arms span was used instead of height was 0.71 and 0.74 respectively.

Conclusions: Based on the results of this study we therefore conclude that arm span measurement is the most reliable physical parameter that can be used to estimate for standing height and can be used reliably as a surrogate for actual measured standing height in the determination of predicted lung volumes during spirometric examinations. *Phil Journal of Chest Diseases. Vol. 14 No. 1. pp: 53-59*

Keywords: Spirometry, prediction equation, arm span length

Introduction

Pulmonary function testing is an important part in the evaluation of many patients referred to the pulmonary department or specialist. Comparing the patient's actual performance to predicted values forms the basis of this evaluation. The age, sex, race and standing height are the variables most frequently used in developing reference values in pulmonary function3. Almost all equations for the prediction of lung functions in various populations include these variables. Of all the physical measurements of the human body, lung function best correlates with standing height.[1-3] However, several patients referred for pulmonary function testing are unable to stand as a result of extreme debility, structural defects (amputees, patients with severe kyphoscoliosis and other thoracic/lumbar spine deformity) or those with neuromuscular weakness.[4] This condition makes the measurement of the standing height

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difficult and inaccurate. The most conventional method of ascertaining height in these cases is to measure the arm span and subsequently estimating height by dividing the measured arm span by a fixed arm span to height ratio which is specific for sex and race.[3] Several investigators proposed to use arm span measurement as a direct surrogate for measured standing height.[1,3,5] Height may also be estimated from arm span using a fixed correction factor or by regression equations.[1,3,9] Although this is not absolutely accurate, the height obtained by such calculations closely approximates measured actual standing height. Previous studies done by Sinclair et al in 1960 and by Hepper et al in 1965 noted that height strongly correlated with arm span and Pearson and Lee in 1992 indicated that normal individuals have only small difference between the measured height and arm span measurement. So we hypothesized that direct substitution of arm span to measured height in the estimations of lung volumes would introduce only a very small error in the interpretation of pulmonary function results. Since there are a lot of patients referred to us in the Department of Pulmonary diseases whose pulmonary function needs to be evaluated but they are bedridden due to severe debility, fractured lower extremities, has severe arthritis or other conditions that deters us from measuring the actual standing height, this study will try to test that hypothesis.

Aggarwal, Gupta and Jindal in 1999 evaluated 228 patients in North India and compared the arm span measurement with that of the actual measured standing height and computed the predicted spirometric measurements including the FEV_1, FVC, FEV_1/FVC ratio and the MEFR. The arm span was measured from the tip of the middle fingers with the hands maximally outstretched, with the subjects standing and facing the wall. The authors concluded that substitution of arm span for height in the prediction equations for lung function introduces only a small error in the calculation of predicted values which is statistically significant and therefore is a reasonable surrogate for measured height.[1] Hibbert and Lanigan in 1988 used the height and arm span measurements in healthy 8-18 year old boys and girls to assess the appropriate correction factor to be applied when height cannot be measured easily. They found out that no correction factor was found necessary and height was directly estimated from the arm span.[5]

Parker, Dillard and Phillips in 1996 prospectively evaluated 202 subjects referred for pulmonary function testing at the Walter Reed Army Medical Center. They tried to evaluate the effects of age, sex, race and the measured arm span for height on the lung volumes. They formulated a set of regression equation that can be used to predict the standing height in those subjects whom this measurement is unobtainable. Height was also be estimated using fixed ratios by dividing a subject's measured arm span by the appropriate ratio for age, sex and age (Estimated Height = measured arm span ratio).

Mohanty et.al.in 2001 did a study on 505 apparently healthy South Indian women in the age group 20-29 were various physical measurements were correlated with actual standing height concluded that arm span measurement was the most reliable body parameter for predicting the height of an individual. It can also be used in predicting age related loss in stature and in identifying individuals with disproportionate growth abnormalities and skeletal dysplasia. It can also be useful in determining alterations in height that occurs due to progressive deformities of the spine and following surgical correction of spinal deformities.[6]

Since spirometry is a vital test used to evaluate the pulmonary function of patients referred to the Department of Pulmonary Diseases, a surrogate parameter to predict actual lung volumes is very important. Since a lot of patients referred for evaluation are elderly with concomitant thoracic/lumbar spine deformities, symptomatic arthritis, fractured lower extremity, neuromuscular disease, severely debilitated who are unable to stand, and height can not be measured accurately. The use of arm span measurement as a direct surrogate for measured standing height for the prediction of lung volumes has been used and evaluated by several authors and have shown to be accurate and statistically sound, although with slight variation with race. If this study can prove that measured arm span can be directly substituted for measured actual standing height for the prediction of lung volumes among Filipino patients at the Veterans Memorial Medical Center, then this would be a welcomed and useful alternative that we can use for our patients.

Several authors mentioned that there is a slight variation in the direct estimation of height using arm span if a fixed correction factor is used or by regression equations. They also mentioned that the correlation of between arm span to height and the predicted lung volumes determined using the two parameters have shown to be different with racial and ethnic groups, gender, age due to the normal anthropometric changes that goes with aging.[1,6] But, there are no present data (local) or similar studies done on this subject among Filipinos and more so among the elderly sub group of the population where such changes are expected. This study is undertaken to test the hypothesis that direct substitution of arm span to measured height in the estimations of lung volumes would introduce only a very small error in the interpretation of pulmonary function

results and see if there is a difference in the correlation between the two parameters among Filipino elderly population.

Methods

This is a prospective, cross sectional study using arm span measurement in the prediction of lung volumes and comparing it with results of the spirometric test when actual measured standing height was used. The study was conducted at the Veterans Memorial Medical Center for a period of one year from July 2003 to July 2004 with a target population of 42 subjects for FEV_1 Expected Difference of Mean between height and arm span (0.159 ±-0.236) and 396 subjects for FVC Expected Difference of Mean at 95% confidence interval (0.81 ± 0.236) at $\alpha = 0.05$ and $\beta = 0.20$. The subjects included in the study were screened for their ability to follow instructions as to minimize inter-subject variability as they were asked to do spirometric test and willing to have their arm span measured. This includes individuals who are 18 yrs old and above whether apparently normal or diagnosed with a pulmonary disease referred to the Department for spirometric test for lung volumes. The subject population also includes all the Medical Staff, Fellows in training, Residents, Post Graduate Interns, and Senior Clerks and Physicians from other Centers currently rotating or training, Nurses, Hospital employees, patients currently admitted or out patients who were referred for spirometry for clearance prior to surgery and routine diagnostic test and individuals who qualified to the above criteria.

Excluded from the study were a) subjects in whom height can not be measured accurately due to presence of structural bone deformities or neuromuscular defects b) subjects with chest or upper limb deformities, who are unable to raise both arms due structural or neuromuscular defects that would make measurement of the arm span inaccurate c) those with maintenance medications who are symptomatic when such medications are withheld for 24 hours are also excluded. Subjects should not take any short acting bronchodilators for the past six hours, 12 hours for long acting bronchodilators and the last 24 hrs for long acting Theophylline as this may affect the results of the spirometric tests.

Arm Span Measurements. The subjects were asked to stand with the back facing the wall and both arms abducted to about 90° with the elbows and wrist extended and palms facing directly forward. The arm span was then measured using a flexible steel tape from the tip of the middle finger of one hand to tip of the middle finger of the other hand of maximally outstretched arms to the nearest centimeter and recorded. Each subject was measured twice, when the two measurements for each parameter agreed to within 0.5 centimeters then the average was taken as the best estimate of the true value.[1,6] The recorded arm span measurement was then used as a variable to compute for the predicted lung volumes (FEV_1 and FVC) for age and recorded.

Height Measurements. The actual standing height was measured to the nearest centimeters with subject standing barefoot on the platform of a standard stadiometer with the upper buttocks and heels pressed against the upright position of the instrument. The subjects head was positioned in the Frankfort horizontal plane and the head plate was brought into firm contact with vertex.[1,6] The measured standing height was then used as a variable to compute for the predicted lung volumes (FEV_1 and FVC) for age and height.

Spirometric determinations of lung volumes. Spirometry was done to determine the following lung volumes a) measured FEV_1 b) % FEV_1 of predicted c) measured FVC d) % FVC of predicted e) FEV_1/FVC ratio using the *MicroLoop* spirometer attached to a microprocessor. The subjects were allowed three trials with the best measurement recorded. The arm span measurement, sex and age were used as variables using the formula by Quanjar et. al (Report Working Party for the Standardization of Lung Function Test 1993)[7,10] to calculate for the predicted value and so with the standing height measurement and compared. Only one technician was asked to perform the spirometry and measure the arm span to minimize operator variability. Spirometry is done in order for us to determine (compute) the predicted lung volumes when arm span is used and compared them with the actual values when actual standing height was used.

The other data collected were as follows: a) Name (initials) b) Gender c) Age d) actual measured standing Height in centimeters, e) Arm span measurement in centimeters, f) Weight in kilograms, g) presence of congenital/structural deformities in the chest wall, spine and the lower extremities h) measured lung volumes.

Statistical Analysis. A two-tailed test was used to analyze paired differences between standing height and arm span measurement. Correlation Analysis was done to determine the relationships of lung volumes with measured actual standing height and arm span. Regression equations for predicting FEV_1 and FVC with age and height as the predictor variables determined while another Regression equation was done by gender.

The predicted FEV_1 for height with age and arm span with age was based on the standardized lung function values reported by the working party of the

Table IV. Relationship of Gender with the different variables when measured using Height and Arm span.

Variables	MALES		FEMALES		P value
	Mean	SD	Mean	SD	
Age	71.78	10.90	69.14	13.21	0.022
Height (cms)	163.29	7.47	151.49	7.67	0.000
FEV_1 Predicted	2.4375	0.5128	1.700	0.4599	0.000
FEV_1 measured	1.5710	0.6066	1.747	6.8768	0.685
% FEV_1	64.80	24.48	74.54	21.05	0.000
FVC Predicted	3.1767	0.5872	2.0705	0.4937	0.000
FVC measured	2.2965	0.6815	1.7068	0.5124	0.000
%FVC	73.27	22.28	82.27	22.78	0.000
FEV_1/FVC ratio	68.04	15.63	74.51	12.41	0.000
Arm Span	163.37	7.69	151.74	8.09	0.000
FEV_1 Predicted	2.4473	0.5225	1.71131	0.4567	0.000
FEV_1 measured	1.8185	3.9162	1.7474	6.8768	0.890
% FEV_1	64.58	24.36	74.60	22.43	0.000
FVC Predicted	3.1887	0.6010	2.0765	0.5039	0.000
FVC measured	2.2965	0.6815	1. 7068	0.5124	0.000
%FVC	72.66	21.38	82.88	23.10	0.000
FEV_1/FVC ratio	68.04	15.63	74.51	12.41	0.000

Table V. Correlation of predicted lung volumes with measured standing Height and Arm span by Gender.

Variables	Height		Arm Span	
	Correlation Coefficient r	P value	Correlation Coefficient r	P value
Height Arm Span	0.794	0.000	0.794	0.000
Males				
FEV_1 Predicted	0.763	0.000	0.791	0.000
FVC Predicted	0.847	0.000	0.865	0.000
Females				
FEV_1 Predicted	0.609	0.000	0.630	0.000
FVC Predicted	0.631	0.000	0.653	0.000

Correlation is significant at the 0.01 level (two-tailed)

European Community for Steel and Coal workers and the formula by made Quanjar et al.[3,4,7] as follows:

For Males: Predicted FEV_1 = [3.953 x Height] - [0.025 x Age - 2.60]

For Females: Predicted FEV_1 = [4.30 x Height] - [0.029 x Age - 2.45].

The predicted FVC for height with age and arm span with age was computed based on the regression equation by Aggarwal et al[1] and the ECCP equations by Quanjar et.al.[3,7,10]

Results

A total of 459 subject were entered into the study, 252 (55%) were males and 207 (45%) were females, the youngest was 19 years old and the oldest was 90 years old with a mean age of 70.59 years (SD = 12.05). For males, age ranged from 27-89 years old with mean of 71.78 years (SD = 10.90 p value = 0.69) and females, age ranged from 19-90 years old with a mean of 69.14 years (SD = 13.21 p value = 0.92) (*Table I*). Most of the subjects entered into the study were elderly (*Table III*) as 81% were 60-90 years old and only 19% were below 60 years old as this Center mainly caters to retired military veterans and their dependents.

The minimum measured standing height was 120 cms and maximum of 183 cms. (*Table I*). The measured standing height among males subjects were slightly higher compared to females which ranged from 120-183 cms with a mean of 163.29 cms (SD = 7.47 p value = 0.47) while for females, measured standing height ranges from 127-180 cms. with a mean 157.26 (SD = 7.67 p value = 0.53).(*Table I*).

The measured arm span for all subjects was slightly higher than the measured standing height which conforms with the review done by previous authors.[1,6,8] The measured arm span ranged from 120-190 cms with a mean of 158.12 cms for both sexes (SD = 9.77) (*Table I*). Male subjects had a slightly higher measured arm span compared to females which ranges from 120-190 cms with a mean of 163.37 cms (SD = 7.69) and female subjects, ranged from 120- 172 cms with a mean of 151.74 cms (SD = 8.09 p value = 0.000 (*Table IV*).

In most subjects, regardless of gender, the mean arm span measurement exceeded measured standing height by only 0.15 cms. which was not statistically significant, although both measurements for males exceeds that of females. The expected discrepancy was not demonstrated in this study even though 81% of the subjects belonged to the 60-90 years old age bracket (*Table III*) since patients with significant spinal column deformity, and other deformities of the peripheral bone structures were excluded. This was done in order to demonstrate the true relationship between measured arm span and measured standing height and if it really approximates height in normal subjects.

Both measured standing height and measured arm span were significantly greater in males as compared to female subjects. However there is no significant difference in the absolute difference between sexes (mean difference of 0.0794 SD=6.01 p value=0.834) for males and (mean difference of 0.25 SD=6.45 p value=0.576) for females (*Table II*). This showed no significant statistical difference and that measured arm span approximates measured standing height. A direct correlation was also seen between the measured standing height and arm span using the Pearson correlation coefficient r=0.794 p value=0.000 (correlation is significant at 0.01 level (2 tailed) which means that there

Table I Descriptive Statistics for all subjects entered into the study.

	Number	Minimum	Maximum	Mean	Standard Deviation
Age	459	19	90	70.59	12.05
Height (ems)	459	120	183	157.97	9.57
FEV_1 Predicted	459	0.90	3.93	2.1049	0.6117
FEV_1 measured	459	0.28	100	1.6505	4.6347
Percent FEV_1	459	17	180	69.19	23.48
FVC Predicted	459	1.20	4.90	2.6778	0.7760
FVC measured	459	0.47	3.94	2.0305	0.6774
Percent FVC	459	20	180	77.33	22.93
FEV_1/FVC ratio	459	29	100	70.96	14.61
Arm Span	459	120	190	158.12	9.77
FEV_1 Predicted	459	0.90	4.35	2.1162	0.6142
FEV_1 measured	459	0.28	100	1. 7864	5.4477
Percent FEV_1	459	18	193	69.10	24.01
FVC Predicted	459	1.19	5.41	2.6871	0.7868
FVC measured	459	0.47	3.94	2.0305	0.6774
Percent FVC	459	20	186	77.27	22.72
FEV/FVC ratio	459	29	100	70.96	14.61

Table II. Comparison of Height and Arm Span measurements by Gender at 95% Confidence Interval.

Gender	Height		Arm Span		Difference		pValue
	Mean	SD	Mean	SD	Mean	SD	
Males (n= 252)	163.29	7.47	163.37	7.69	0.0794	6.01	0.834
Females (n=207)	151.49	I 7.67	151.74	8.09	0.25	6.45	0.576

Table III. Age distribution of subjects entered into the study.

Patient Age	Males 252 (55%)	Females 207 (45%)	Total 259
< 20 yrs	0	2	2 (0.43%)
20-29 yrs	1	0	1 (0.21%)
30-39 yrs	0	3	3 (0.65%)
40-49 yrs	14	20	34 (7.40%)
50-59 yrs	27	15	42 (9.15%)
60-69 yrs	29	39	68 (26.25%)
70-79 yrs	126	87	212 (46.18%)
80-89 yrs	55	40	95 (20.69%)
90 & above	0	1	1 (0.21%)

is a strong correlation between arm span measurement and standing height. The measured standing height to measured arm span ratio for both sexes was equal to 1.000495.

A direct correlation was shown using the Pearson correlation coefficient between actual measured standing height and measured arm span which was r= 0.794 (*Table V*) which was comparable to the review done by Steel and Chenier in 1990 among black women at r= 0.852 and r= 0.903 for whites. It was also the same in the study done by Mohanty et. al. in 2001 which was at r= 0.816 among young Hindu women from South India aged 20-29 years old.

Measured standing height and arm span was directly correlated with the FEV_1 (*Table V*) for both males and females which was also comparable to the previously mentioned reviews. When correlation was done between genders, for males r = 0.763 p value= 0.00 for height and r = 0.791 p value = 0.000 for arm span and females r = 0.609 p value = 0.000 for height and r = 0.630 for arm span measurement. (*Table V*). All correlations were significant at *p=0.01* level (two-tailed test).

A direct correlation was also seen in the predicted FVC when actual measured standing height r=0.915. By Gender, among males r=0.847 p value=0.000 using height and r=0.865 p value=0.000 when arm span was used. Among females r=0.631 p value=0.000 for actual standing height and r=0.653 *p=0.000* for measured arm span (*Table V*) was also seen. All correlations for FVC were significant at 0.05 level (two-tailed test). The expected difference in the anthropometric measurements seen with aging (81% of the subject population were elderly) was not demonstrated in this study as there is a direct correlation between measured arm span and measured standing height r=0.974 p value=0.000.

A regression equation was derived from the above data for the prediction of normal lung volumes are as follows:

Using measured standing height:

Males - FEV_1 Predicted = [1.90 - 0.025 (Age)] + [0.036 (Height)]

Females - FEV_1 Predicted = [1.07 - 0.030 (Age)] + [0.027 (Height)]

Using measured Arm span:

Males - FEV_1 Predicted = [0.636 - 0.0325 (Age)] + [0.0284 (arm span)]

Females - FEV_1 Predicted = [0.776 - 0.0258 (Age)] + [0.0784 (arm span)]

Discussion

The measurement of height is important for the determination of basic energy requirements, standardizations of measurements of physical capacity

like the determination of lung volumes and for adjustments in drug dosage.[6] However, there are situations that the exact standing height can not be measured accurately because for certain deformities of the limbs, those who had undergone amputation and those with severe debilitating conditions and are unable to stand. In such circumstances, an estimate of the height has to be computed based on other body parameters. Several studies have reported the effectiveness of using various body parameters in predicting height and arm span measurement was found to be the most reliable.[1,5,6,8] However the association was found to vary from race to race, between sexes and probably with age due to the normal anthropometric changes that goes with aging.

Several authors attempted to estimate height using the different physical measurements. In 1985, Chumlea et.al. estimated stature from knee height while Mitchel et al in 1982 used arm length measurement as an alternate to height in assessing the nutritional status among elderly patients and found a positive correlation that it can be used as an alternate to height. In 1965, Hepper and co-workers first attempted to use arm span as substitute for height in determining lung volumes among normal subjects and compared to patients with spinal deformity and reported a strong correlation.[1]

In 1990 Steele and Chenier studied black and white women in the age group 35-89 reported a good correlations of measured arm span and height of r=0.852 and F=0.903 for black and white women respectively. Aggarwal and Gupta in 1999 reported a correlation of F=0.779 for arm span and r=0.808 for height which is about the same as the one reported by Mohanty et. al in 2001 of F=0.816. All these results were similar to the correlations obtained in the present study which shows an F=0.794. The resulting predicted values for FEV_1 and FVC when computed using measured arm span correlates well with predicted values when actual measured standing height was used and the absolute differences (*t-test* for equality of means) in the various predicted values using the two parameters were small and statistically insignificant. Based on the above results we contend that using arm span measurement is the most reliable indirect physical measurement for estimating height and can be used as a surrogate for determining lung volumes when such measurements for height can not be made accurately. Although there were previously reported racial, ethnic, gender and age differences in the arm span to height measurements this was not demonstrated in this review since the results were comparable to such studies.

Conclusion

Of all the physical measurements of the human body, arm span measurement is the most reliable physical parameter that can be used to estimate height when its measurement is not possible or unreliable. The predicted lung volumes determined with the use of measured arm span as variable introduces only a very small absolute difference when compared to lung volumes determined using actual measured standing height which was statistically insignificant. Based on the results of this study we therefore conclude that arm span measurement can be used reliably as a surrogate for actual measured standing height when such measurements is not possible in the determination of predicted lung volumes.

Recommendations

Since this Center caters to the elderly sub group of the population were patients have various physical deformities or in chronic debilitated state attributed to aging and disease and standing height can not be measured accurately for lung volume determination, adjustments of drug dosage or computation of nutritional requirements. Arm span should be used as surrogate for height in the wards, pulmonary laboratory and other areas in the hospital. Secondly, the standard used in the predicting lung volumes during spirometry in the VMMC pulmonary laboratory (Knudson) has been used since the sixties and is deemed obsolete and is a standard based on Caucasian subjects which give erratic results when used among smaller Filipinos. A normal standard for ventilatory function test among adult Filipinos was done by Roa et.al way back in 1987 may be used as standard reference values.[9]

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Validity of Fiberoptic bronchoscopy in the diagnosis of Bronchogenic Malignancies

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Background: Lung Cancer is the leading cause of cancer death for both men and women worldwide. Chest radiograph has been a valuable tool in the early detection of bronchogenic cancer. Fiberoptic bronchoscopy is being widely used for its diagnosis.
Objectives: This study will correlate the diagnosis of bronchogenic carcinoma based on specific descriptions of lesions through fiberoptic bronchoscopy to the histopathologic report by Pap's smear and cell block after biopsy, bronchial washing and brushing.
Methodology: This was a prospective cross sectional study done in 116 patients admitted at the Veterans Memorial Medical Center from January 2004 to January 2005 with chest radiographic findings suggestive of malignancy. They were subjected to fiberoptic bronchoscopy regardless of age, sex and symptoms. The gross bronchoscopic descriptions were noted and the diagnoses based on these findings were made. All subjects with bronchoscopic findings suggestive of bronchogenic carcinoma were correlated with the histopathologic results. Patients with negative histopathology after bronchial biopsy were further subjected to other means of diagnostic modality such as trans-thoracic needle aspiration (TTNA) biopsy, video-assisted thoracoscopic surgery (VATS) with biopsy or open thoracostomy; whichever was most feasible for the pulmonary lesion. Finally, the incidence of various cytological examinations by bronchoscopy (bronchial washing, brushing and tissue biopsy) was determined to evaluate the diagnostic power of each of these in bronchogenic carcinoma.
Statistical Analysis and Results: Sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) measures of validity were determined. The rate of positivity was measured using frequency and percent distribution. Kappa test was used to determine the significance of agreement of the different diagnostic procedures with the gold standard. A $p<0.050$ was considered significant. The cross-tabulation of the different diagnoses via description of gross bronchoscopic lesions and histopathologic diagnosis using the Kappa co-efficient showed that there is an agreement between the two variables [Kappa: 0.326 and p<0.000). Among the four different cell types of Bronchogenic carcinoma, this study identified 87.5% of Squamous cell Carcinoma (specificity: 88.1%), 66.7% of Small cell Carcinoma (specificity: 79.3%) and 53.3% of Adenocarcinoma lesions (specificity: 92.2%) through fiberoptic bronchoscopy as validated by histopathology. None was identified as Large cell Carcinoma. This study show that bronchial wash, brush and forceps biopsy are good diagnostic tools in obtaining specimen that would yield a high rate of positivity for malignancy (p<0. 000). Bronchial wash is the least diagnostic and has a very low sensitivity of 37.9%, as compared to 85.2% for bronchial brush. Forceps biopsy is the most diagnostic with 92.3% sensitivity, 100% specificity, 100% PPV and 93.3% NPV.
Conclusion: An agreement was found between description of lesions of the different types of Bronchogenic Carcinoma and histopathologic findings, and is found to be valid. Majority (87.5%) of Squamous cell Cancer, 66.7% of Small Cell Cancer and 53.3% of Adenocarcinoma lesions were identified through fiberoptic bronchoscopy as proven by histopathology. Large cell Carcinoma is a diagnosis of exclusion. No significant association was found between gender and the risk of acquiring malignancy. Likewise, no significant relationship was found between age and the occurrence of malignancy. This study shows that bronchial wash, brush and forceps biopsy are good diagnostic tools in obtaining specimen that would yield a high rate of positivity for malignancy. Bronchial wash, however, is the least among the three, with sensitivity of 37. 9%. Bronchial brush is far better than bronchial wash, and forceps biopsy, in general, is the most powerful tool in diagnosing Bronchogenic malignancies. *Phil Journal of Chest Diseases. Vol. 14 No. 1 pp: 60-67*

Keywords: Bronchogenic carcinoma, fiberoptic bronchoscopy, diagnosis

Introduction

Lung Cancer accounts for approximately 6% of all deaths in the United States each year, and is the leading cause of cancer death for both men and women. Lung Cancer like most other solid tumors is unfortunately, usually recognized late in its natural history. The five-year mortality from the time of presentation remains at approximately 85% to 90%.

Of 100 newly presenting patients with lung cancer, 80 patients will be inoperable at presentation and approximately 20 patients will proceed to attempted resection, of which 5 to 10 patients will be alive 5 years later.[1] The chest radiograph has been a valuable tool in

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the early detection of bronchogenic cancer. Some patients who have radiographic findings of mass lesion that is central in origin or peripheral or some patients who present with hemoptysis are subjected to other diagnostic procedures such as bronchoscopy. There are a lot of studies concerning sensitivity of the different cytologic examinations during fiberoptic bronchoscopy for endoscopically visible lung cancer. However, there were no studies as of yet concerning comparison between gross bronchoscopic description of lesions pathognomonic of bronchogenic cancer and histopathologic result in patients suspected 0f bronchogenic carcinoma.

This study will correlate the diagnosis of bronchogenic carcinoma based on specific description of lesions through fiberoptic bronchoscopy to the histopathologic report by Pap's smear and cell block after biopsy, bronchial washing and bronchial brushing.

Methodology

Study Design/Sample Size/Scope This was a prospective cross sectional study done in 116 patients admitted at the Veterans Memorial Medical Center from January 2004 to January 2005 with chest radiographic findings suggestive of malignancy and were subjected to bronchoscopy regardless of age, sex and symptom.

Assuming that the incidence of negativity for malignancy (Bronchogenic cancer) is 40%, α = 0 05, computed after a review of the logbook of patients who underwent video-bronchoscopy at VMMC from January to July 2003, the estimated sample size at total width of Confidence Interval of 20% is $\geq$ 92 patients.

Chest Radiograph Evaluation. The chest radiographs of all patients were evaluated by the pulmonary fellows-in-training and team consultants. Any density noted on chest radiograph located at any zone of the lung that is suspicious of malignancy whether primary or metastatic, or even presence of a solitary pulmonary nodule, was subjected to bronchoscopy for evaluation.

Bronchoscopy preparation. All patients who were medically cleared were scheduled for bronchoscopy. The procedure was explained to all patients and informed consent was secured. Thirtv minutes prior to the procedure, each subject was given diphenhydramine 50mg intramuscular or intravenous, followed by nebulization using either salbutamol or ipratorium plus salbutamol. Local anesthesia using 2% Lidocaine was given.

Fiberoptic Bronchoscopy. The gross bronchoscopic descriptions were noted and the diagnosis based on these findings were made: (a form was provided for each patient). The following were noted:

For Squamous cell carcinoma: Redness of mucosa nodular polypoid cauliflower-like; For Adenocarcinoma: extramural compression at the carina or bronchial bifurcation, irregularity on the longitudinal folds, indistinct cartilage crescents, engorged sub-epithelial vessels; For Large cell carcinoma: necrosis, mucosal irregularity, vascular engorgement, ulcer formation; For Small cell carcinoma: (preserved bronchial epithelium): submucosal changes, swelling, redness, marked subepithelial vascular engorgement, bronchial stenosis

The principal investigator was present during the procedure to check the bronchoscopic findings. Bronchial washing, brushing and forceps biopsy were done to all patients as the need required, after which, the specimens were brought to pathology for Pap's smear and cell block.

All bronchoscopy procedures were videotaped and were reviewed by the principal and supervising investigators every end of the week (Fridays) to assure that there was uniformity on the descriptions of the bronchoscopic lesions.

Gathering of Results. At the end of the study, all data were gathered and all subjects were segregated as to positive or negative bronchoscopic findings of bronchogenic carcinoma. All subjects with bronchoscopic findings suggestive of bronchogenic carcinoma were correlated with the histopathologic results. We looked for the agreement between the presence of malignancy by description of bronchoscopic lesion and the histopathologic diagnosis. Association with normal bronchoscopic findings and histopathologic results were also done to look for the incidence of negative findings on bronchoscopy that eventually turned out to have a positive histopathologic result.

Eventually, all results that turned out to be positive for malignancy by bronchoscopy, with its specific lesions descriptive of a particular histologic type of cancer (squamous cell carcinoma, Adenocarcinoma, small cell carcinoma and Large cell carcinoma) were compared to the histopathologic report and evaluated for agreement.

Patients with negative histopathologic results after bronchial biopsy were further subjected to other means of diagnostic modality such as transthoracic needle aspiration (TTNA) biopsy, video-assisted thoracoscopic surgery (VATS) with biopsy or open thoracotomy, once confirmed, whichever was most feasible and accessible for the pulmonary lesion.

Table I Characteristics of patients.

Characteristics	(+) Malignancy by Histopathology (n=30)	(-) Malignancy by Histopathology (n=86)	P Value
Mean Age years (± SD)	66.97 (15.09)	67.90 (10.63)	0.189
Sex, n (%) Male (89, 76.7)	26 (29.21)	63 (70.79)	0.134
Female (27, 23.30)	4 (14.8)	23 (85.20)	

Table II. Agreement between FOB findings and Histopathology results (n, %).

FOB Finding	(+) Histopathology	(-) Histopathology
Positive 59 (50.86)	24 (40.68)	35 (59.32)
Negative 57 (49.14)	6 (10.53)	51 (89.47)
TOTAL 116 (100)	30 (25.86)	86 (74.14)

Sensitivity	80%
Specificity	59.3%
PPV	40.7%
NPV	89.5%

Finally, the prevalence of the various cytological examinations by bronchoscopy (bronchial washing, bronchial brushing and tissue biopsy) was determined to evaluate the diagnostic power of each of these in bronchogenic carcinoma.

Statistical Analysis. Sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) were determined to measure validity. The rate of positivity was measured using frequency and percent distribution. Kappa test was used to determine the significance of agreement of the different diagnostic procedures with the gold standard. A $p < 0.05$ was considered significant.

Results

Patient Demographics. There were a total of 116 subjects included in the study. Among these, 30 (25.86%) were positive and 86 (74.14%) were negative for malignancy by histopathologic examination via fiberoptic bronchoscopy with specimen obtained from bronchial washing, brushing and forceps biopsy. Of the 30 subjects with positive malignancy, 26 (29.21%) were males and four (14.80%) were females; and of the remaining 86 subjects with negative malignancy, 63 (70.79%) were males and 23 (85.20%) were females.

Based on the result of the statistical analysis, there was no significant association between gender and acquiring malignancy ($p=0.134$). The mean age for the subjects with positive malignancy by histopathologic examination was 66.97 (± 15.09), while 67.90 (± 10.63) for the subjects with negative malignancy, indicating that there is no significant relationship between age and occurrence of malignancy, $p=0.189$ (*Table I*).

Table II shows that, of the 116 subjects included in the study population, there were a total of 59 subjects (50.86%) whose description of gross bronchoscopic lesion was malignant, while 57 subjects (49.14%) were negative grossly (i.e., those with normal bronchoscopic findings, or others that cannot be described as malignant such as metastatic changes and inflammatory changes).

Among the 59 subjects with positive FOB, 24 were positive by histopathologic examination (PPV: 40.68%) and 35 (59.32%) turned out to be negative (false positive). On the other hand, among the 57 subjects with negative FOB, six (10.53%) turned out to be positive by histopathology (false negative), and 51 (Specificity: 59.3%) remained negative. The sensitivity of FOB in detecting Bronchogenic Carcinoma is 80%.

Agreement of Bronchoscopic Findings with Histopathologic Diagnosis: (Table III). Among the 57 subjects with negative bronchoscopic findings, 51 were negative after histopathologic evaluation. The remaining six showed positive result for malignancy. Of the six positive, one was Squamous cell Carcinoma, one was Large cell Carcinoma, three were Adenocarcinoma, and there was one subject who showed a combination of Small Cell CA and Adenocarcinoma on histopathologic examination, making a total of 58 histopathologic reports for the said variable; and with 117 as total number of reported histopathologic results for this study.

Table III Agreement between bronchoscopic findings and histologic diagnosis

Bronchoscopic Findings, n	*Negative on Histopathology, n (%)*	*Squamous cell CA on Histopathology, n (%)*	*Small cell CA on Histopathology, n (%)*	*Adeno CA on Histopathology, n (%)*	*Large cell CA on Histopathology, n (%)*	*Specificity, %*
Negative, 58	*51 (59.3)*	*1*	*1*	*4*	*1*	
Squamous cell CA, 20	*9*	*7 (87.5)*	*1*	*2*	*1*	*88.1*
Small cell CA, 23	*18*	*0*	*4 (66.7)*	*1*	*0*	*79.3*
Adeno CA, 16	*8*	*0*	*0*	*8 (53.3)*	*0*	*92.2*
Large cell CA, 0	*0*	*0*	*0*	*0*	*0*	
Total, 117	*86*	*8*	*6*	*15*	*2*	

Kappa = 0.326 p=0.000

Table IVa Agreement between Bronchial wash and Histopathology results

Bronchial Wash	(+) Histopathology	(-) Histopathology	Total
Positive	11	0	11
Negative	18	86	104
Total	29	86	115
Sensitivity	37.9%		
Specificity	100%		
PPV	100%		
NPV	82.7%		

Table IVb Agreement between Bronchial brush and Histopathology results

Bronchial Brush	(+) Histopathology	(-) Histopathology	Total
Positive	23	0	23
Negative	4	46	50
Total	27	46	73
Sensitivity	85.2%		
Specificity	100%		
PPV	100%		
NPV	92%		

Table IVc Agreement between Bronchial biopsy and Histopathology results

Bronchial biopsy	(+) Histopathology	(-) Histopathology	Total
Positive	12	0	12
Negative	1	14	15
Total	13	14	27
Sensitivity	92.3%		
Specificity	100%		
PPV	100%		
NPV	93.3%		

Of the 59 subjects diagnosed to have Bronchogenic malignancies based on their gross bronchoscopic lesions, 20 were Squamous cell Carcinoma, 23 were Small cell Carcinoma, 16 were Adenocarcinoma and none was described as Large cell Carcinoma.

Among the 20 Squamous cell Carcinoma via fiberoptic bronchoscopy, seven were Squamous cell Carcinoma on histopathology (specificity: 88.1%), two were Adenocarcinoma, one was Small cell Carcinoma and one was Large cell Carcinoma. The remaining nine were negative for malignancy.

Of the 16 Adenocarcinoma via fiberoptic bronchoscopy, eight were Adenocarcinoma on histopathology (specificity 92.2%) and the remaining eight were negative for malignancy.

Finally, of the 23 Small cell Carcinoma via fiberoptic bronchoscopy, four were Small cell Carcinoma on histopathology (specificity: 79.3%) and one was Adenocarcinoma. The remaining 18 were negative for malignancy.

The cross-tabulation of the different diagnoses via description of gross bronchoscopic lesions and histopathologic diagnosis using the Kappa test showed that, there is an agreement between the two variables. This means that the diagnosis made by bronchoscopy through the description of gross lesions agree with the histopathology result, and is significant. (Kappa coefficient: 0.326 and one-tailed $p = 0.000$)

In this study, the sensitivity of fiberoptic bronchoscopy in detecting Squamous cell Carcinoma was 87.5% while the specificity was 88.1%. For small cell carcinoma the values are 66.7% sensitive and 79.3% specific for Small cell Carcinoma; and for Adenocarcinoma, 53.3% sensitivity and 92.2% specificity. There were no lesions for Large cell Carcinoma.

Agreement of Various Cytological Studies with Histopathology. One hundred fifteen subjects underwent bronchial washing on FOB. Eleven of these had gross bronchoscopic findings of malignancy and 11 subjects revealed positive for malignancy on histopathology. The remaining 104 had negative FOB; however, the histopathologic examination report showed that 18 were positive for malignancy (*Table IVa*)

Seventy three subjects underwent bronchial brushing on FOB. Twenty three of these had gross bronchoscopic findings of malignancy. On histopathologic examination, they all revealed positive for malignancy. Of the remaining 50 subjects who were negative on bronchoscopy, four were reported to have malignancy on histopathologic examination (*Table IVb*).

Twenty seven subjects underwent forceps biopsy on FOB. Twelve had gross bronchoscopic findings of malignancy and 15 had negative FOB. On histopathologic examination, all 12 positive FOB subjects showed positive findings of malignancy, and one of the 15 negative FOB subjects turned out to be positive (*Table IVc*).

Not all subjects underwent bronchial brushing and forceps biopsy. This is for the very reason that, some lesions were very friable, such that, merely a touch of the tip of the scope would have the lesion bleed: hence, bronchial washings alone were done. All lesions including those with normal bronchoscopic findings had bronchial washing except one.

This study shows that bronchial wash, bronchial brush and forceps biopsy are good diagnostic tools in obtaining specimen that would yield a high rate of positivity for malignancy ($p < 0.000$). However, bronchial wash is apparently the least among the three. It has a very low sensitivity of 37.9% as compared to

Table V. Distribution of patients with positive malignancy on histopathology and non-malignant findings by bronchoscopy

Bronchoscopy Findings	Squamous cell CA	AdenoCA	Small cell CA	Large cell CA	Total
Negative	0	2	1	0	2
Endobronchitis	1	2	0	0	3
Extraluminal compression, etiology (?)	0	0	0	1	1

Table VI Association of other diagnostic procedures with Histopathologic findings

Procedure	Positive Histopathology	Negative Histopathology	Total
Transthoracic Needle Aspiration biopsy (TTNA)	13 (86.67%)	2 (13.33%)	15
Video assisted thoracoscopic surgery with biopsy (VATS)	1 (50%)	1 (50%)	2
Open thoracostomy with biopsy	0	0	0

Table VII Association of Bronchoscopic findings with Histologic diagnosis by TTNA

Bronchoscopy Findings	Squamous cell CA	Small cell CA	Adeno CA	Large cell CA	Others	Total
Squamous cell CA	1		1			2
Small cell CA		2	1	1		4
AdenoCA			6	1		7
Large cell CA						0
Normal			1			2
Total						15

85.2% and 92.3% for bronchial brush and forceps biopsy, respectively.

Bronchial brush and forceps biopsy are better procedures in obtaining specimen that would give a high yield of positivity for malignancy. Forceps biopsy, as shown, is the best procedure with 92.3% sensitivity, 100% specificity, 100% PPV, and 93.3% NPV. The results of this study support other data published, attesting that biopsy, in general is the most powerful tool in diagnosing Bronchogenic Malignancies.

Other Salient Findings It will be interesting to note that there were six non-malignant findings via fiberoptic bronchoscopy, at which after histopathologic examination eventually turned out to be positive for malignancy.

They might have appeared normal or benign grossly when viewed via a bronchoscope, but the biopsy specimens showed the presence of malignancy. In fact, there was one patient with normal bronchoscopic findings who showed a combination of Small Cell Carcinoma and Adenocarcinoma on histopathologic examination.

Furthermore (*Table VI*), an association of other diagnostic procedures with the histopathologic findings showed that; subjects whose histopathologic results were negative after FOB, or with gross lesions suggestive of a specific cell type of malignancy but with negative histopathologic results; when further subjected to Transthoracic Needle Aspiration Biopsy and Video-assisted Thoracoscopic Surgery with Biopsy, eventually revealed to Bronchogenic Malignancies. Of the 17 subjects with negative histopathologic results after FOB, 13 showed malignancy after being subjected to trans-thoracic needle aspiration biopsy and one after video-assisted thoracoscopic surgery with biopsy. Similarly, shown in *Table VII* are the histopathologic results of the 13 subjects believed to have lesions descriptive of a particular cell type of Bronchogenic Malignancy by FOB but with negative histopathologic results that turned out to be truly malignant only after TTNA.

Tables VI and VII tell us that a combination of diagnostic procedures (FOB with TTNA/VATS/Open thoracostomy) will greatly help clinicians to objectively arrive at a more accurate diagnosis for clinically and radiographically suspected bronchogenic carcinomas that are of diagnostic dilemma.

Discussion

More than 90% of patients with Lung Cancer will be asymptomatic at presentation. The diagnosis is usually suspected following a chest radiograph. The chest radiograph plays a pivotal role in the recognition of Lung Cancer. However, it is useful to appreciate that clues from chest radiograph may not only suggest the diagnosis of Lung cancer but may also point toward the histologic subtype. Like chest radiography, there are also descriptions of bronchoscopic lesions that point toward a specific histologic subtype.

For squamous cell carcinoma as it appears on the bronchoscope, redness of the mucosa and vascular engorgement are remarkable. The bronchoscopic findings are divided into three: 1) Superficial: redness of the mucosa, 2) Nodular: the invasion is beyond the bronchial cartilage and 3) Polypoid: extremely small lesions with very limited invasion or may show deep invasion through the bronchial wall. Furthermore, it has been well-documented that in well-differentiated squamous cell carcinoma, a mass that has a cauliflower like appearance accompanied by bleeding and necrosis is noted from the orifice.

For Adenocarcinoma, the most recognized are advanced cases. Most recognizable findings on bronchoscopy are due to lymph node metastasis which can cause extramural compression primarily at the carina and at the bronchial bifurcation. Irregularity can be seen in the longitudinal folds and there is indistinctness of the cartilage crescents and engorgement of the subepithelial vessels.

For Large cell carcinoma, features of both poorly differentiated Adenocarcinoma and squamous cell carcinoma, particularly the former, can be recognized. Presence of necrosis, mucosal irregularity, vascular engorgement and ulcer formation at the site of the primary lesion may be recognized.

And, finally, for Small cell carcinoma, lymph node is frequently more prominent than the primary lesion. Submucosal changes, swelling, redness, marked subepithelial vascular engorgement and remarkable bronchial stenosis can be seen. Unlike squamous cell carcinoma, bronchial epithelium is well preserved.[25]

The cross-tabulation of the different diagnoses via description of gross bronchoscopic findings and histopathologic diagnosis using the Kappa coefficient showed that there is an agreement between the two variables for Squamous cell carcinoma, Small cell carcinoma, Adenocarcinoma, and normal tracheobronchial findings. This means that the diagnosis made by bronchoscopy through the description of gross lesions agree with the histopathology, and the result is significant (Kappa coefficient: 0.326 and one tailed *p=0.000*). However, fiberoptic bronchoscopy could hardly identify the lesions descriptive of Large cell carcinoma.

In this study, the following bronchoscopic descriptions for each of the different cell types that were pathognomonic are described below.

For Squamous cell carcinoma, it is the presence of nodular, polypoid and cauliflower-like lesions. For Adenocarcinoma, the presence of extramural compression involving the carina and the bronchial bifurcation and irregularities on the longitudinal folds were pathognomonic. For Small cell carcinoma, the presence of submucosal changes, marked subepithelial vascular engorgement, and bronchial stenosis (fish mouth opening) with a preserved bronchial epithelium indicated this type. For Large cell carcinoma, it is often a diagnosis of exclusion because features of both poorly differentiated Adenocarcinoma and squamous cell carcinoma, particularly the former, can be recognized. This could be the reason why it was very difficult to say that the lesion is of the Large cell type, hence, in this study, no gross lesion for Large cell Carcinoma through fiberoptic bronchoscopy was described.

A comprehensive literature search on studies published since 1970 was performed to determine the sensitivity of FOB for the diagnosis of bronchogenic cancer. Eight studies were identified that reported on the sensitivity of bronchoscopy (brush and/or biopsy for peripheral lesions with a size less than 2cm or greater than 2cm in diameter.[15-17,21] The sensitivity for peripheral lesions < 2cm in diameter was 0.33. Peripheral tumors with a diameter > 2cm resulted in a sensitivity of 0.62. Likewise, six studies[7,8,17,22-24] reported on the sensitivity of post-bronchoscopy sputa as an adjunct to the previously mentioned bronchoscopic techniques, as 0.35. In our study, post-bronchoscopy sputa, was no longer included as a variable.

Among the four different cell types of Bronchogenic carcinoma, this study identified 87.5% of squamous cell carcinoma (specificity: 88.1%), 66.7% of small cell carcinoma (specificity: 79.3%) and 53.3% of Adenocarcinoma lesions (specificity: 92.2%) through fiberoptic bronchoscopy as verified by histopathology. None was described as large cell carcinoma. The decreasing frequency of distribution could be explained by the fact that the central lesions (Small cell and Squamous cell carcinoma) have higher over-all sensitivity (88%)[2-12] for all bronchoscopic modalities combined, than that of the peripheral diseases, Adenocarcinoma and Large cell carcinoma (69%).[4,5,8,11-16]

Thirty studies of patients with central disease were identified to determine the sensitivity of bronchoscopy with central diseases.[2-12] Endobronchial biopsies provide the highest sensitivity (0.74) followed by brushings, (0.59) and washings (0.48). the interpretation of the sensitivity for bronchogenic aspirates (range, 0.23 to 0.90; average 0.56) was limited to fewer studies with large differences in sample size and inconsistencies in technique (i.e., endobronchial or transbronchial biopsies). The overall sensitivity for all bronchoscopic modalities combined, where reported, was 0.88 for centrally located endobronchial disease

Thirty studies reported on the sensitivity of flexible bronchoscopy beyond the visual segmental bronchi.[4,5,8,11-16] Fifteen of these studies showed that brushings provided the highest sensitivity (0.52), followed by transbronchial biopsies (0. 46) in 18 studies and BAL washings (0.43) in 13 studies. Although TBNA had a high sensitivity (0.67; 5 studies), the data deserve cautious interpretation because of the limited number of studies and large differences in sample size.

In 12 studies, the over-all sensitivity for all modalities in the diagnosis of peripheral disease was 0.69.

This study shows that bronchial wash, bronchial brush and forceps biopsy are all good procedures in obtaining specimen that would yield a high rate of positivity for malignancy (p=0.000), whether the disease is central or peripheral. However, bronchial wash is apparently the least among the three. It has a very low sensitivity of 37.9% as compared to 85.2% and 92.3% for bronchial brush and forceps biopsy, respectively. Bronchial brush and forceps biopsy are better procedures in obtaining specimen that would give a high yield of positivity for malignancy.

Forceps biopsy is the best diagnostic tool with 92.3% sensitivity, 100% specificity, 100% PPV and 93.3% NPV. The results of this study support other data published, attesting that biopsy, whether transbronchial or endobronchial, is the most powerful tool in diagnosing bronchogenic malignancies.

Conclusion

At the end of the study, an agreement was found between description of lesions of the different cell types of Bronchogenic Carcinoma and histopathologic findings, and was found to be valid. Among the different cell types of Bronchogenic carcinoma, this study identified 87.5% of Squamous cell Cancer, 66.7% of Small cell Cancer and 53.3% of Adenocarcinoma lesions through fiberoptic bronchoscopy as proven by histopathology. Large cell Carcinoma is a diagnosis of exclusion.

No association was found between gender and the risk of acquiring malignancy. Likewise, no significant association was found between age and the occurrence of malignancy.

This study shows that bronchial wash, bronchial brush and forceps biopsy are good diagnostic tools in obtaining specimen that would yield a high rate of positivity for malignancy. However, Bronchial wash is the least among the three with sensitivity of 37.9%. Bronchial brush is far better than bronchial wash with sensitivity of 85.2%. Forceps biopsy in general is the most powerful tool in diagnosing bronchogenic malignancies with 92.3% sensitivity, 100% specificity, 100% PPV and 93.3% NPV.

This pilot study could serve to enhance the efficacy of fiberoptic bronchoscopy in our institution, and in others as well.

Limitations

The main limitation of the study is the small sample size. Although the results of the study were significant, there should have been more subjects included.

Recommendations

A follow-up study on validation of bronchoscopic description of the different cell types of Bronchogenic Carcinoma with the gold standard – histopathology - is recommended. Although the results of the study were significant, the data deserve cautious interpretation because of the limited number of studies available and differences in sample size. Lastly, to allow collection of an adequate number of sample sizes a longer time frame of study is necessary.

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Sputum Smear Conversion among Sputum Acid-Fast Bacilli (AFB) Smear Positive Patients given Fixed dose Combination chemotherapy at Veterans Memorial Medical Center DOTS Tuberculosis Clinic

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Objectives*:* To determine whether the Fixed-Dose Combination Chemotherapy in a directly observed setting is effective in achieving the cure rate of 85% as targeted by the WHO and the National Tuberculosis Program (NTP) and to investigate whether age, gender, or chest x-ray findings correlate with time to culture conversion.

Methodology*:* The study is a prospective, cohort study involving smear-positive TB patients who are more than 15 yrs of age with no previous anti-TB treatment or received said drugs for less than one month who underwent directly-observed therapy. Excluded were patients with any of the following characteristics: body weight < 30 kg, known or suspected hypersensitivity to any of the 1st line medications, known adverse reactions to anti-TB medications which would preclude its use, and use of immunosuppressive drugs during the course of treatment. Age, gender, and chest radiographic findings of each of the patients were noted. Sputum AFB smears were monitored at day 60, day 120, and day 180 of treatment.

Statistical analysis*:* Percentage of patients whose sputum AFB smears converted to negative in each of the periods specified (days 60, 120,180). Cure rate is computed by taking the percentage of subjects who converted at the end of treatment, which is on day 180.

Results*:* Twenty-five eligible participants were included in the study but six dropped out. Out of the remaining 19 patients, 13 (68.4%) were males while 6 (31.6%) were females. Mean age was 36 ± 14 years. One out of twenty-four had atypical chest x-ray result. Among the typical radiographic report, seven had cavitary lesions while 12 had non-cavitary lung disease. Smear conversion was 94.7% at day 60, 100% at day 120, and 100% at day 180. The computed cure rate was 100% which surpassed the target rate of 85%.

Conclusion*:* The fixed-dose combination chemotherapy administered using directly-observed treatment achieved a 100% cure rate. However, the small number of subjects set a limit to this conclusion. Original investigator's plan to correlate age, gender, and radiographic report with time was not done due to inadequate population. The median time to conversion is placed at day 60. A more frequent smear determination would have provided a more specific period at which conversion is observed. *Phil Journal of Chest Diseases. Vol. 14 No. 1 pp: 68-71*

Keywords: Pulmonary TB, chemotherapy, treatment

Introduction

Sputum AFB smear together with chest radiography constitute the diagnostic tools of Pulmonary TB. Although sputum AFB culture is the gold standard in PTB diagnosis, the cost and the lack of laboratory facilities limit its use in selected groups of patients in developing countries like the Philippines. Instead sputum AFB smear, which is less expensive and technically easier to perform, is recommended in establishing the diagnosis and monitoring treatment outcomes of PTB. The absence of AFB in the sputum smear does not rule out the diagnosis of PTB. A positive sputum AFB smear, however, especially if occurring twice in three determinations or if coupled with a chest x-ray finding suggestive of TB, indicates a highly infective TB state (smear-positive TB). Arresting its spread by starting immediate appropriate treatment, assuring good compliance, and monitoring on a regular basis are the thrusts of TB treatment.

The most recent WHO report (2004) provided an estimate of incidence of 8.8 M new cases of TB worldwide in 2002 based on trends in case notification. Among these 3.9 M were smear-positive. The number of

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Table I. Demographic data of participants (N=25)

Patient factors	
Age	36 ± 14 yrs old
Gender	
Male	13
Female	6
Chest Radiograph result	
Typical	24
cavitary	10
noncavitary	14
Atypical	1

Table II. Sputum AFB smear conversion based on scheduled sputum monitoring

Days from the onset of treatment	Percentage of patients with sputum conversion
Day 60	94.7%
Day 120	100%
Day 180	100%

cases is growing at 2.4% per year.[1] The Philippines, one of the high burden countries, stands 8th in the global rank. The incidence of new smear positive cases in the country is placed at 144/100,000 population. Mortality per 100,000 population is placed at 57.[1] The figures provide us with a vivid picture of the large load of the health system in controlling this infectious disease. Left untreated, each person with active TB will infect on average between 10-15 individuals yearly.[2]

The first aim of the study is to determine whether the fixed-dose combination chemotherapy in a directly observed setting is effective in achieving the cure rate as targeted by the WHO and the NTP by determining the rate of sputum AFB smear conversion in six months and determining the median time to sputum AFB smear conversion. Secondly, we will identify whether the following patient factors correlate with time to smear conversion: age, gender, and chest radiograph results

Methodology

Subjects. Participants were taken from pulmonary tuberculosis patients who were registered at the VMMC TB Clinic from June 2003 until December 2003. Included were patients who were at least 15 years old with either at least two sputum AFB smear positive results on microscopy or one sputum AFB smear positive report and a chest radiographic finding that is consistent with pulmonary tuberculosis, and absence of anti-TB treatment or less than a month of previous treatment if present. Excluded were individuals with any of the following characteristics: body weight of less than 30 kg, with known or suspected hypersensitivity to any of the first line anti-TB medications, known adverse reaction to anti- TB meds which would preclude its use and immunosuppressive therapy during the course of treatment.

Study Design. The study was designed as a prospective cohort study. Eligible participants visited the clinic monthly for regular check-up and their sputum were monitored every two months until they reach the end of treatment, which is usually at six months depending on the result of the sputum exams. The treatment regimen consisted of two months of intensive treatment with a fixed-dose combination of Isoniazid/Rifampicin/Pyrazinamide/Ethambutol and maintenance phase of treatment of four months with a fixed-dose combination of Isoniazid and Rifampicin. Treatment regimens would have variations in the event of persistent smear positivity at each follow-up period. Sputum AFB smears were reported as positive or negative for AFB organisms. The schedule of request for sputum exam is done as recommended in the National TB Program of the Department of Health.[3] The age, gender, and chest radiography findings were noted for each individual. Typical tuberculosis chest x-ray includes those with apical infiltrates and cavitary lesions while atypical findings are any finding that excludes the characteristic ascribed to typical result.

Statistical Analysis. The numbers of patients with sputum smear conversion at two months (Day 30), four months (Day 120), and at six months (Day 180) were counted. Cure rate were computed at each of the three scheduled days by noting the number of patients who converted at each different periods. The computed numbers were compared against the target cure rate for TB which is 85%.

Results

A total of 25 eligible participants were entered into the study. Out of these, six did not complete the study due to the following reasons: hypersensitivity reaction to the medication (2), transfer to another treatment center (2), lost to follow-up (2). Of the remaining 19 patients, 13 were males (68.4%) and 6 (31.6%) were females Age ranged from 16-60 years old, with a mean age of 36 ± 14 yrs. atypical chest x-ray report, which was read as right hilar infiltrates, was noted in only one patient. Seven had cavitary lesions on radiology while 12 had non-cavitary result. Eighteen had smear conversion, that is, sputum smear became negative (94.7%) at 60 days. On the 4th month (120 days) of smear determination, on 17 patients were included in the analysis because 2 patients have not reached this period in their course of treatment. At 120 days into the treatment, 100% the population had

negative AFB smears. At Day 180, only 12 patients were counted with results because the remaining five patients have not reached this point in their treatment. All of the 12 patients had negative AFB smears (100%).

There was no statistical presentation of relationship of age, gender, and radiographic results. There was only one patient who did not respond on the 60th day of treatment. However, it was noted that all patients had conversion after 180 days of treatment regardless of the above-mentioned factors. This observation was not conclusive due to the very small number of patients who completed the follow-up period.

Discussion

With the attainment of the WHO goal of detecting 70% of Tuberculosis and achieving a cure rate of 85% of TB cases by year 2010, at least a quarter of TB cases and a quarter of TB deaths may be prevented in the next two decades.[4]

The result of the study was able to demonstrate that the VMMC TB DOTS clinic was able to surpass the cure rate level that the WHO aimed to meet. The main factor that explains this success is the good treatment compliance of the subjects that involves the assistance of a treatment partner, usually a family member, who supervises and monitors the daily intake of the anti-TB drug. Add to this is the reminder of the schedule of missed follow-up visit made by the clinic staff.

The study, however, failed to enroll the required number of subjects that is necessary to state more definite conclusions. The computed sample size at the onset of the study was 49 as against 25 subjects that the study was able to gather. Only 1 out of 19 cases (94.7%) had persistent positive sputum smear by the second month of treatment. We attributed this to missed doses of the medications during the intensive phase of treatment. The median time to smear conversion in the present study would be at day 60. Determining the median time may be more accurate if more frequent monitoring of the sputum bacteriology will be performed. However, the paucity of financial resources makes this plan not feasible.

The use of fixed-dose combination chemotherapy, that is anti-TB drugs formulation in a single tablet, as opposed to loose tablets, has been present for more than 40 years in the market. Only three years ago, however, did the WHO and the IUATLD recommend its use as a means to promote better treatment adherence.[5] The fixed-dose combination chemotherapy offers a simpler approach to TB management both for the practitioner and the patient as it makes prescription of medications easier and avoids missed intake of medications since lesser number of drugs are used. Taken on a larger scale, this would curtail the practice of some physicians to recommend inappropriate drug regimens and prevent the rise in cases of drug-resistance. The limitation identified in the use of fixed-dose combination chemotherapy in this study is that it can not be used in cases of hypersensitivity reaction. Two out of the 25 cases discontinued the said drug formulation due to intolerable pruritus and rashes that were not responding to antihistamines. The general occurrence of adverse drug reactions to anti-TB medications, however, is only 3-6%[6] and the literature noted rare instances of true hypersensitivity reactions to isoniazid, rifampicin, pyrazinamide, and ethambutol.[6,7]

The persistence of sputum culture positivity at the second month of treatment identifies patients at high risk for treatment failure or relapse. The study intended to establish correlation between age, gender, chest x-ray findings (whether typical or atypical of PTB, and either cavitary or non-cavitary lung lesion) and duration before smear conversion. Due to the small population of the study, this analysis was not possible. In a retrospective study of smear positive pulmonary tuberculosis patients admitted to a referral hospital and who received standard short-course chemotherapy under direct observation, age groups 41-60 and more than 60 yrs old, numerous bacilli on initial sputum smear examination, and presence of multiple cavitary diseases were significant factors correlated with persistent sputum smear positivity at the second month of treatment.[8] Cavitary lung disease, in one study, was associated with prolonged conversion time.[9] ·In another local study involving individual drug formulations under DOTS program, age, gender, presence or absence of cavitary lung lesions are not correlated to duration prior to sputum culture conversion.[10]

Conclusion

The cure rate using the fixed-dose combination chemotherapy at the VMMC TB Clinic using directly-observed therapy is 100%. The median time to conversion is 60 days. Correlation between age, gender, and chest x-ray findings and duration before sputum AFB smear conversion was not done due to the limited number of subjects.

Limitation

The small population enrolled into the study limited the data necessary to make a significant conclusion. A large proportion of the smear-positive patients encountered in the outpatient and inpatient settings have received previous anti-TB treatment. The recruitment of patients into the study is hampered by this setback. Add

to this is the ongoing treatment and sputum monitoring of seven patients which led to their exclusion in the analysis of smear conversion at particular periods. The original intention of the investigator to perform a more frequent monitoring of the sputum AFB smear during the initial phase of the treatment where smear conversion is likely to occur was not carried out due to financial constraints.

Recommendation

A longer time for patient recruitment and follow-up period could have provided a more significant conclusion to the study.

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Sleeping Patterns of Residents in Training at the University of the Philippines – Philippine General Hospital (UP-PGH) as Measured by the Epworth Sleepiness Scale (ESS)

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Background and Objectives: Sleep has always been an important aspect of human life, an important component of mammalian homeostasis, vital for the survival of self and species. Excessive daytime sleepiness (EDS) and consequently a reflection of sleep deprivation in the general community is a newly recognize problem, about which there is little standardized information. Prevalence of EDS is common among several occupations including medical students and medical trainees. However, the literature describes few studies on excessive daytime somnolence among these subjects whose activities entail a lack of sleep as well as too much work. This study is the first in our country with a primary aim of determining the prevalence of daytime sleepiness among the residents in training and possibly presents a more varied data with regard to sleeping patterns of adults who primarily work in a health related environment.

Study Design: Cross-Sectional, Cohort

Participants: All residents-in-training in the following departments: Medicine, Family and Community Medicine, Surgery (including Neurosurgery), Obstetrics-Gynecology, Pediatrics, Emergency Medicine, and Neurosciences; and a cohort of 45 age-matched office workers who worked during daytime only (8 AM to 5 PM) were given a self-administered questionnaire. The questionnaire included the Epworth Sleepiness Scale (ESS) and questions on sleeping habits and patterns.

Analysis: The data collected was analyzed according to the Epworth Sleepiness Scale (ESS) scoring system. Statistics done were mostly descriptive to elucidate the general characteristics of the subjects. ANOVA and t-test with $p < 0.05$ were used to correlate for differences between groups with their mean ESS scores.

Results: 277 residents and 45 controls responded. Prevalence of EDS, i.e. mean ESS score > 10, among residents was 90.5% compared with control, 26.7% (p=0.000). Mean ESS score was 12.3 compared to control with mean ESS of 8.3, (p=0.000). Sleepiness was most noticeable among lower year level residents (p=0.007) and those with prolonged duties (p=0.000). No statistical difference was noted across departments, age and sex. 73.6% had sleep duration $\leq$ 6 hours. More than half (57%) had 1-3 awakenings per night mostly secondary to emergency room/ward calls. Most of the residents felt sleepy during the day (87.9%) and still feel unrefreshed (87.2%) after a night's sleep. Nearly half (45.7%) took naps while 67.2% had at least 2 cups of methylxanthine containing beverages within the 24-hr period. Nearly two-thirds (61%) did not need any method to help them fall asleep; however, 1.4% reported use of sleep aid medications. None took any medications to keep them awake.

Conclusions: EDS among the residents was highly prevalent. EDS was primarily brought about by sleep loss secondary to prolonged working hours and sleep fragmentation leading to circadian rhythm disturbances. However, fatigue and other stresses could not be discounted. Further studies are recommended to test for cognitive function, psychomotor performance and other work related learning and personal health variables to further address the sleep deficiency experienced by our residents. These may have an impact on one's performance and patient care, not to mention its academic repercussions. *Phil. Journal Chest Diseases. Vol 14 No. 1 pp: 72-78*

Keywords: Residents, sleepiness, training

Introduction

Sleep has always been an important aspect of human life, but its scientific exploration began only 70 years ago.[1] It is an important component of mammalian homeostasis, vital for the survival of self and species. Humans spend at least one third of their lives asleep, yet have little understanding of why sleep is needed and what mechanisms underlie its capacities for physical and mental restoration.[2] Excessive daytime sleepiness and consequently a reflection of sleep deprivation in the general community is a newly recognize problem, about which there is little standardized information.

In general population surveys, excessive daytime sleepiness (EDS) is a fairly common complaint.[3]. However, the literature describes few studies on excessive daytime somnolence in occupations such as drivers, night shift workers, medical residents as well as medical students, whose activities entail a lack of sleep as well as too much work.[4] In a study of all Americans,

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excessive daytime sleepiness as a public health problem is prevalent by almost 12%.[5] Excessive somnolence in the general population has a prevalence of about 10 - 20%[6] to as high as 25.2% in a recent report.[3]

The Epworth Sleepiness Scale. The individual subjective reports of sleepiness are generally imprecise compared to observer reports or objective tests of sleepiness.[1] Thus, several objective and formal subjective measures have been devised to quantify the degree of individual's sleepiness. The *Epworth Sleepiness Scale (ESS)* is one of them and is currently the most utilized subjective test of daytime sleepiness in clinical practice. First published in 1991, it was designed to measure subjective sleep propensity and global level of sleepiness as it occurs in common life situations.[8] It is most useful in clinical practice in assessing daytime sleepiness. It distinguishes feeling asleep from just feeling tired. The advantages of the ESS aside from it being validated, is its reliability in assessing subjective sleepiness and ability to distinguish normal patients from patients with sleep disorders. It is the most useful in clinical practice in assessing daytime sleepiness because it relates to common life situations. Its disadvantages however, lies on its inability to determine short term acute sleep loss and it cannot be used on multiple occasions throughout the day.[8,9] ESS is a standard, low cost, quick and easy to apply scale. It has been validated comparing to the gold standard of EDS which is Multiple Sleep Latency Test (MST), with a high internal consistency, measured by Cronbach alpha index (0.88).[3,10] ESS focuses the various tendencies of excessive sleepiness, with eight questions, encompassing daily monotonous life activities. In the ESS, the subjects are instructed to rate the chance of dozing off or falling asleep in eight different life situations varying in their soporific nature using an evaluation window of a few weeks.[8,11] Scores are computed according to Epworth Sleepiness Scale Score. A score of $\leq$ 8 indicates normal sleep function, 8 - 10 indicates mild sleepiness, 11 - 15 indicates moderate sleepiness, 16 - 20 indicates severe sleepiness and a score of 21 - 24 indicates excessive sleepiness. A score of 10 is defined as upper limit of normal, while a score greater than 10 signifies excessive daytime sleepiness.[8]

Excessive Daytime Sleepiness among Medical Trainees and its Implications. Prolonged working hours during residency training is a time-honored tradition. Most resident physicians have wrestled with long hours of work lasting to 70 to 100 hour work weeks and as much as 36 hour night shifts.[12] For the past two decades, studies on effects of sleep loss and fatigue in the context of medical training has generated interests as well as controversies.[13] Most where appraisals regarding sleep loss and fatigue and its varying effects on both the residents and its repercussions with regards to patient care and the individual trainee. The SAFER (Sleep, Alertness and Fatigue Education in Residency),[14] a program created by the American Academy of Sleep Medicine has pooled several facts on the effects of sleep loss among residents in training. Several studies reviewed by the committee have shown effects of sleep deprivation in specialties, across individual tasks and its repercussions on patients and residents safety and on medical education. To cite a few examples, in surgery, 20% more errors and 14% more time are required to perform simulated laparoscopy post-call. Internal Medicine (IM) residents on the other hand, had exhibited impairment in ECG interpretation among sleep deprived interns. On the other hand, 58% of ER residents reported near crashes. Among anesthesia residents, 20% indicated that sleepiness prevented them from performing clinical duties and 12% of them attributed commission of errors due to fatigue. The committee concluded that depression, drowsiness and fatigue is an element of any residency training and may be equated to be impairment just like alcohol and drugs.

Furthermore, two recent studies reported that residents who had an average of more than 80 work hours per week were more likely to be involved in personal accident or injury, serious conflicts with fellow staff, making significant medical error, as well as more likely to use alcohol, use medications to stay awake, and exhibited noticeable weight change.[15,16]

A related report cited several documented studies on which sleep deprivations affects resident performance ranging from cognitive tasks, language, memory and numerical skills, monitoring of anesthesia, memory retention and problem solving, as well as its effects on visual attention, concentration and coding ability. Not to mention other ill effects on one's physical and emotional make-up as well as the family strain that it created.[12] Another study among Internal Medicine residents, reported that 51% of the mistakes they had was caused by too many other tasks and 41% attributed it primarily to fatigue.[17] A recent multi-institutionalized study among residents described multiple adverse effects of sleep loss on fatigue, ranging from effects on professionalism and task performance, personal well-being and relationships with spouse and other members of the family. Most (84%) of them had exhibited ESS scores in which clinical intervention is indicated.[18]

In spite of the importance of these facts, a scarcity of data can be found in Asian literature with regards to EDS among resident trainees. In our country, few

Table I. Distribution of study population by department

Department	Total population	Respondents (%)
Surgery	70	45 (55.7)
Medicine	61	51 (83.6)
Obstetrics-Gynecology	57	48 (84.2)
Pediatrics	82	43 (52.4)
Neurosciences	15	10(66.7)
Emergency Medicine	]0	9 (90)
Neurosurgery	7	6 (85.7)
Family Medicine	35	26 (74.3)
Office workers	-	45
Total Number of Residents	337	232(68.8)
Total Number of Respondents	-	277

Table II. Demographic data of study population

Parameter	Data(%)
Sex (N=275)	
Male	97(35.3)
Female	178(64.7)
Missing data	2
Mean Age (N=277)*	
Residents	28.2 years
Office workers	27.8 years
Missing data	4
Year Level (N=232)	
1	75(32.3)
2	71 (30.6)
3	54(23.3)
4	21(9.1)
5	10(4.3)
6	1(0.4)

* Age range is 21 - 41 years for all respondents

sleep studies in general has been done with regards EDS. Most were in relation to Obstructive Sleep Apneas. In fact, no study yet, as to the best of our knowledge, has been done in our country with regards sleeping patterns and excessive somnolence among medical residents.

This study is the first in our country using the Epworth Sleepiness Scale (ESS) and a self-administered questionnaire on sleep habits with a primary aim of determining the prevalence of daytime sleepiness among the residents in training and possibly presents a more varied data with regard to sleeping patterns of adults who primarily work in a health related environment.

Methodology

Study Design: Cross Sectional, Cohort

Study Setting: UP- Philippine General Hospital Medical Center

Study Population: 1) Residents-in-training in the following departments: Medicine, Family and Community Medicine, Surgery (including Neurosurgery), Obstetrics-Gynecology, Pediatrics, Emergency Medicine, and Neurosciences; 2) an age-matched group of office workers.

Inclusion Criteria: All residents-in-training in the enumerated departments.

Exclusion Criteria: The researchers and those who were on leave or not willing to participate.

Procedure. All residents of the above mentioned departments were given a self-administered questionnaire. The questionnaire included the Epworth Sleepiness Scale (ESS) and questions on sleeping habits and patterns. A cohort of 45 age-matched office workers who worked during daytime only (8 AM to 5 PM) were also given the questionnaire.

Statistical Methods. The data collected was analyzed according to the Epworth Sleepiness Scale (ESS) Scoring system. Statistics done were mostly descriptive to elucidate the general characteristics of the subjects. t-test and ANOVA with $p < 0.05$, were used to correlate for differences between groups with their mean ESS scores.

Results

Three hundred thirty seven residents from eight departments and 45 age matched daytime shift workers were given the self-administered questionnaire. Two hundred thirty two (68.8%) of the residents and all of the office workers answered the questionnaire. (*Table I*)

The mean ages of the subjects were 28.2 years and 27.8 years for residents and office workers, respectively (range 21 - 41). Most (64.7%) were females and, among the residents (86.2%), belong to the first three years of residency (*Table II*).

The residents with the highest mean ESS was surgery (13.2) followed by OB-Gyne (12.9) and Pediatrics (12.2). The department with the least means ESS was neurosciences (10.7). The mean ESS of all departments were higher than 10, signifying on the average, residents had excessive daytime sleepiness. As a whole all residents had a mean ESS of 12.3. There were no significant differences among departments with regards to mean ESS. (*Table III*).

Table III. Daytime sleepiness among residents

Department	Mean ESS score (SD)	P value
Surgery	13.2(4.8)	0.371[a]
OB-Gyne	12.9(4.4)	
Pediatrics	12.2(3.9)	
Medicine	11.9(3.6)	
Emergency Medicine	11.8(3.4)	
Family Medicine	11.6(4.2)	
Neurosciences	10.7(1.9)	
All Residents *(N=232)*[+]	12.3(4.1)	
Office Workers (n=45)[#]	8.3(3.6)	0.000[b]

[a] ANOVA result between different departments
[b] t-test result between all residents compared to office workers
[+] 90.5% has ESS score >10
[#] 73.3% has ESS score < 10 (26.7% has ESS score > 10)

Table IV. Daytime sleepiness among year levels

Year Level (N=232)	Mean ESS score (SD)	P value
1	12.9(4.4)	0.007
2	12.8(3.5)	
3	11.9(3.2)	
4	9.4(4.1)	
5	12.3(6.7)	
6	8.3(5.8)	

Table V. Frequency distribution of subjects according to different sleep variables with their mean ESS scores

Variables	Frequency (%)	Mean ESS score (SD)	P value
Length of duty (N=276)			0.000
> 24 hrs [a]	34(12.8)	12.7(4.8)	
Every 3 days [a]	127(47.7)	12.5(3.8)	
Every 4 days	28(10.5)	10.0(3.5)	
no 24 hrs[b]	58(21.8)	9.51(4.6)	
Once a week	19(7.14)	12.1 (3.9)	
Missing data	1		
Sleep duration (N=277)			0.102
< 3 hrs*	22(7.8)	13.1(3.8)	
3.1 - 4*	33(11.9)	13.0(4.9)	
4.1 – 5*	75(27.1)	11.5(4.4)	
5.1 – 6*	77(27.8)	10.9(3.9)	
6.1 - 7.9	44(15.9)	11.2(4.3)	
> 8	26(9.4)	12.3(3.8)	
Number of awakenings per night (N=277)			0.458
None	73(26.4)	12.2(4.8)	
1-3	158(57.0)	11.6(4.1)	
4-10	34(12.3)	11.0(4.3)	
>10	10(3.6)	12.6(2.9)	

[a] 60.5% had approximately >80 working hours per week
[b] 13 residents and all office workers had no 24 hr duty
* 73.6% had sleeping time of less than or equal to 6 hrs

The office workers had a mean ESS of 8.3. Thirty three (73.3%) of them had a score of less than 10. On the other hand, 90.5% of residents had an ESS score of greater than 10. These are significantly different from each other. (*Table III*)

Table V shows the frequency distribution of subjects according to different sleep variables with their mean ESS scores. Subjects who went on duty more than 24 hours, those who go on duty once a week and every three days had significantly higher mean ESS as compared with those who never go on duty and those who go on duty every four days. The mean self reported sleep duration for residents is 5.35 hours while that of office workers is 6.33 hours. This is statistically significant ($p = 0.000$). Most (73.6%) of the residents had a sleep duration of less than or equal to six hours. Mean ESS is not significantly different among various ranges of sleep duration.

Majority of residents (126/230) and office workers (32/45) are awakened from one to three times at night. On the extreme, 10 subjects were awakening more than ten times each night. The most frequent reason for waking up was ER or ward calls (41.5%). This was followed by going to the toilet (32%) and noise (32%). (*Table VI*)

Table VI shows the subjects methods to aid them to sleep or keep them awake. Majority of the subjects (61%), did not need any methods to aid them to sleep and about 39% need to do things to help them go to sleep. The most common methods used were reading, watching TV and listening to music. Only 1.4% needed to take medications, mostly pain relievers, antihistaminics and anxiolytics. None took any meds to keep them awake.

Table VII shows the consequences of having the subjects' current sleeping habits. The residents were significantly sleepier during the day as compared to office workers (87.9% vs 64.4%). Likewise, there were more residents who wake up either still tired and somewhat refreshed (87.2%) as compared to office workers (60%). This is significant when compared with office workers. Many (45.7%) find time to take a nap which is not significant when compared with office workers. Most (67.2%) also took at least 2 cups of methylxanthine containing beverages.

Discussion

Sleepiness and fatigue is common among medical personnel, particularly among resident physicians.[18-20] Working for long-hours is a tradition during residency and intemship[21] with most of them working beyond 80 hours a week and on several occasions working continuously for greater than 36 hours.[15] During these times, their sleep may be interrupted by a variety of factors, ranging from ER/ward calls to personal needs.

Several assessment tools have been developed to measure sleep propensity among individuals: Multiple

Table VI. Frequency distribution of subjects on reasons for waking up, methods/aids used to aid them to sleep or be awake

Variable	Frequency
A. Reasons for waking up	
ER/ward calls (N=277)	115(41.5)
Toilet (N=277)	97(32)
Noise (N=277)	57(20.6)
Feed baby / child wakes up (N=277)	13(4.7)
Others (N=277)	32(11.6)
B. Methods to aid them to sleep	
Read (N=277)	126(45.5)
Watch TV (N=277)	61 (22)
Listen to music (N=277)	7(2.5)
Others (N=277)	15(5.4)
No methods used (N=277)	108(39)
C. Take Meds to help asleep (N=277)	4(1.4)
D. Take meds to keep awake (N=277)	0

Table VII. Frequency distribution on the consequences of the subjects' current sleeping habits

Variables	Frequency (%)		p value
	Residents	Office workers	
Feel sleepy during the day (N=277)	204(87.9)	29(64.4)	0.000
Feeling after a night's sleep (N=275)			0.000
Refreshed	27(11.8)	18(40)	
Somewhat refreshed*	105(45.8)	16(35.6)	
Still tired*	95(41.4)	11(24.4)	
Missing data	2	0	
Naps (N=277)	106(45.7)	14(31.1)	0.099
Intake of methyl xanthine containing beverages (N=277)			0.226
0	26(11.2)	3(6.7)	
1 cup	50(21.6)	15(33.3)	
2-3 cups	91(39.2)	19(42.2)	
> 4 cups	65(28)	8(17.8)	

* 87.2% of residents felt unrefreshed after a night's sleep

Sleep Latency Test, Stanford Sleepiness Scale and the Epworth Sleepiness Scale (ESS). Our study utilized the ESS in assessing sleep propensity among medical residents.

The prevalence of excessive daytime sleepiness (EDS) in resident physicians in western countries is about 84%.[18] Our study showed a relatively higher prevalence rate of about 90.5%. About 9.5% of our residents showed within the normal range of ESS score (ESS score less than 10) almost comparable (16%) with the study done among residents in various specialties at five academic health centers in the United States.[18] On the other hand, EDS prevalence in the general population ranges from 6.7% to 25.2%,[3] much lower than that observed among physicians undergoing residency training. The comparable EDS prevalence between Filipino and western residents reflect the similar conditions which they work. The difference between residents and the general population indicate the fewer rigors the non-medical personnel are exposed to. In a study among Filipino office workers in a primary care setting, EDS was noted to be 38%.[22] These differences reflects the different working conditions among the non-medical subjects who are not experiencing prolonged working hours. It is important to note, that residents in the first three years of training had higher EDS as compared to more senior residents. This suggests that the former had presumably more workload and consequently less hours of sleep.

On the other hand, no significant correlation was seen with EDS with regards to age, gender and specialty. This is in agreement with the different studies done on EDS.[3,18] This presumably is due to a variety of reasons that may govern the occurrence of excessive daytime sleepiness among different populations. Sleep just like food is a necessity for life. Studies would show that an average 8 hours sleep is needed, for an individual to function well.[14,19]

According to several studies, less than five hours of sleep will manifest in an individual as decline in mental abilities. Even short periods of sleep debt for just a couple of days can result into slower response time and decreased initiatives.[19] Staying awake for just 24 hours straight is equivalent to legal intoxication of 0.10 percent alcohol-level, enough to impair one's performance.[23]

In this study, majority exhibited a range of 4 - 6 hours of daily sleep. Most (60.5%) had an average of two to three 24-hour duties per week. This roughly translates to approximately more than 80 working hours per week. In a study among first and second year residents, 20% of them had an average sleep per night of less than 5 hours, and 66% had 6 hours or less.[16] Higher ESS scores being seen in those residents catering to bigger population of patients and those requiring skills, could be attributed to shorter sleep time, but fatigue could not be ruled out.[24]

Majority (57%) had a range of 1-3 awakenings. This could reflect circadian rhythm "adaptation" of residents when it comes to daily duties and responsibilities. Another reason is the possibility of numerous micro arousals that is not recognized by the individual. The residents therefore have a more fragmented sleep pattern. Napping is relatively common among individuals with shift works. This is a way to combat fatigue. More so, it has been found out to compensate for daytime sleep deprivation and could bridge the night time low point in each individual's sleep.

Majority of the residents (87.9%) feel sleepy and tired during the day compared to office workers. In spite of this only around 46% of the subjects took naps during the day. This could represent a high level of sleep requirement combined with a high level of arousal states.[25] Also, some may have misjudged their sleepiness.

The relative wide range of ESS scores in all the subjects is consistent with the report of Johns,[8] that some healthy adults, without recognizable sleep disorders remain sleepier than others during the day. It connotes that sleep propensity of a subject on a particular day would be influenced by the quality and duration of prior sleep or sleep deprivation. More so, it may depend on the specific time of day, the level of interest and motivation by the situation at hand as well as longer term physiological disturbances.[8]

Sleepiness during the day is a common occurrence for those who have lack of sleep. Some would try to combat sleepiness by stimulants and various kinds of medications to keep them awake. Almost 90% of our residents had at least a cup of methylxanthine containing beverage in a day. Though caffeinated drinks are known to increase arousal states, it has a drawback of disrupting subsequent sleep and tolerance may develop.

The use of various kinds of medications and other hypnotic substances is reported to be about 18% among Americans aged 18-45 y.o. and 5% used it as sleep aides.[26] Our study had a low prevalence of 1.4% with regards to intake of sleep aid medications. Likewise about 61% did not need any methods to aid them to sleep. None of the subjects took any meds to keep them awake. However, there is no clear-cut association with regards to use of medications and the occurrence of daytime sleepiness in this study.

The varied sleep characteristics of our residents in this study points out to interplay of several factors that may have affected one's sleeping habits. It should be noted that since sleepiness is subjective and differs from individual to individual, a given individuals perceived degree of sleepiness and the true objective drive for sleep represent different sleep requirements.[27] It is of note that whether somebody will fall asleep, feel sleepy, or show physiological signs of sleepiness or experience vigilance problems, appears to depend on the level of sleep need or sleep drive unique for each individua1.[25] Moreover, the role of environmental factors could be a prime factor that govern one's level of arousal or wake drive.

Conclusion

Prevalence of excessive daytime sleepiness (EDS) among our residents was 90.5%, relatively higher compared in western literature. Sleepiness was most noticeable among lower year level residents and those with prolonged duties. Moreover, ESS scores were much higher compared to office workers. However, no statistical difference was noted across departments, age and sex which are consistent across studies reported in literature. Majority (73.6%) had sleep duration of less than or equal to 6 hours which is much less to the recommended minimum sleeping time. Disturbances in sleep where primarily brought about by ER/ward calls. Most of the residents feel sleepy during the day and feel unrefreshed after a night's sleep but despite of this, only less than 50% took naps. Majority had at least a cup of methylxanthine containing beverages within the 24hr period. Some attempted some aids to help them to sleep; however, only 1.4% reported use of sleep aid medications.

The excessive daytime sleepiness experienced by the residents could be an inevitable consequence of sleep loss and fatigue. This is primarily brought about by prolonged working hours, shorter sleep time and sleep fragmentation leading to disruptions in the normal circadian rhythms of the individual. Fatigue and other forms of stress however, could not be discounted. The data gathered in this study is consistent with the facts presented by the United States S.A.F.E.R. (Sleep, Alertness, and Fatigue Education in Residency) program on sleep loss and fatigue among residents in training, i.e. sleepiness, drowsiness and fatigue abounds in any residency training program.

With the facts presented, there may be a need to review the current working patterns that our residents are currently experiencing. We believe that it is manageable.

There may be a need to develop strategies to manage sleepiness and fatigue among the trainees. This can be done by having a shared responsibility towards fatigue management as well as use of alertness management and support systems in the training program. Further studies are recommended to test for cognitive function, psychomotor performance and other work related learning and personal health variables to further address the sleep deficiency experienced by our residents, which in effect may have an impact on one's performance and patient care, not to mention its academic repercussions. Moreover, further testing in other training institutions is recommended. This is to determine if these results are consistent across different training institutions in our country.

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Perioperative Predictors for Prolonged Postoperative Mechanical Ventilation after Cardiac Valvular Surgery at the Philippine Heart Center

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Duration of postoperative mechanical ventilation has been used as an objective measure of postoperative pulmonary complication in previous studies. The purpose of this study is to identify the typical duration of postoperative mechanical ventilation in patients undergoing surgical correction of valvular defects in rheumatic heart disease and identify the preoperative, intraoperative and postoperative factors that are associated with PMV (postoperative mechanical ventilation).

This study is a cross sectional retrospective cohort conducted at the Philippine Heart Center, Quezon City, Philippines. A review of medical records of patients with age 19 years old and above, who underwent cardiac surgery for correction of valvular heart disease at the Philippine Heart Center for the period of January 2004 to December 2004 was done. Peri-operative variables were recorded and divided into Preoperative factors: age, sex, height, weight, body mass index, co-morbid illnesses, smoking history, echocardiography, pulmonary function test, cardiac diagnosis, number of valves involve; Intra-operative factors: surgical procedure, duration of surgery, cardiopulmonary bypass time, presence or absence of intraoperative event (e.g., cardiac arrest, massive hemorrhage necessitating multiple blood transfusion); and Postoperative factors: postoperative bleeding within 24 hours post operatively necessitating multiple blood transfusion and/or surgical exploration to control the bleeding, postoperative pulmonary complications such as atelectasis, pneumonia, pulmonary congestion/edema, bronchospasm, pleural effusion, pneumothorax, prolonged mechanical ventilation and failed extubation, and total number of hospitalization days and number of hospital days postoperatively. Patients were allocated to two groups based on the duration of postoperative mechanical ventilation: group 1 (< 24 hours) and group 2 (> 24 hours)

Results showed that 85% of patients were extubated in less than 24 hours postoperatively with no extubation failure reported, 14% were extubated within 24 to 72 hours postoperatively with one (0.9%) patient died after two weeks due to severe sepsis. Preoperative variables did not significantly correlate with prolonged PMV. Among intraoperative variables, duration of surgery and number of blood products transfused during operation correlated well with prolonged PMV. Post operative complications occurring within 24 hours that correlate significantly with prolonged PMV are pulmonary congestion, pleural effusion and unstable arrhythmia. Total duration of hospitalization was also significantly longer in patients who had prolonged PMV.

In conclusion, the most patients (85%) undergoing valvular surgery can be extubated within 24 hours postoperatively. However, preoperative factors are not enough to predict outcome as measured by PMV. Intraoperative and immediate postoperative events are better predictors of prolonged PMV on these patients. *Phil Journal of Chest Diseases. Vol. 14 No. 1 pp: 79-83*

Keywords: Mechanical ventilation, Cardiac surgery, complications

Introduction

Postoperative pulmonary complications are the most common complications observed after cardiothoracic surgery. According to one review, pulmonary complications were at least as common as or more common than cardiac complications in 17 of 25 studies of postoperative complications.[1] Postoperative complication is defined as an abnormality that produces identifiable disease or dysfunction, is clinically significant and adversely affect the clinical course. These include complications either known to prolong the hospital stay or known to be responsible for morbidity and mortality. Several published studies have different definitions for postoperative pulmonary complications and include complications that have no clinical significance. Others authors have used the duration of

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postoperative mechanical ventilation as an objective measure of postoperative pulmonary complication. Although the exact definition of prolonged mechanical ventilation (PMV) is controversial, most studies on patients who have undergone coronary artery bypass defined PMV as those needing mechanical ventilation > 24 hours postoperatively,[2] although some investigators used the 48 - hour cut off.

In coronary and bypass graft surgery (CABG), the reported incidence of PMV (> 24 hours) after first and re-operation CABG is 5.6% and 10.7%, respectively.[2] PMV increases duration of ICU as well as hospital stay, and resource utilization.[3] Therefore, risk stratification for PMV is an important part of the peri-operative evaluation. A number of peri-operative scoring systems have been devised to predict pulmonary complications in cardiac surgery particularly CABG. However, one problem with these existing models is clinical applicability. Most incorporate objective parameters (e.g., PFT) that are not routinely ordered or readily accessible. Sometimes, performance of a particular PFT is contraindicated in a subset of patients.

The purpose of this study is to identify the typical duration of postoperative mechanical ventilation in patients undergoing surgical correction of valvular defects in rheumatic heart diasease and identify the preoperative, intraoperative and postoperative factors that are associated with PMV.

Materials and Methods

Study Design. This study is a cross sectional retrospective cohort conducted at the Philippine Heart Center, Quezon City, Philippines.

Data Collection. A review of medical records of patients with age 19 years old and above, who underwent cardiac surgery for correction of valvular heart disease at the Philippine Heart Center for the period of January 2004 to December 2004 was done. Perioperative variables were recorded. Preoperative variables were: age, sex, height, weight, body mass index, co-morbid illnesses, smoking history, echocardiography, pulmonary function test, cardiac diagnosis and number of valves involve. Intraoperative variables were: surgical procedure, duration of surgery, cardiopulmonary bypass time and presence or absence of intraoperative event (e.g., cardiac arrest, massive hemorrhage necessitating multiple blood transfusions). Postoperative variables were: postoperative bleeding within 24 hours post operatively necessitating multiple blood transfusion and/or surgical exploration to control the bleeding, postoperative pulmonary complications such as atelectasis, pneumonia, pulmonary congestion/edema, bronchospasm, pleural effusion, pneumothorax, prolonged mechanical ventilation and failed extubation. Total number of hospitalization days and number of hospital days postoperatively were also examined. Patients were allocated to two groups based on the duration of postoperative mechanical ventilation: group 1 (< 24 hours) and group 2 (> 24 hours)

Definition of Postoperative Pulmonary Complications. *Atelectasis* - radiographic finding of at least a sub segmental infiltrate or volume loss in the absence of clinical or laboratory signs of infection. *Pneumonia* - new or progressive infiltrate on chest X ray with fever and leukocytosis > 10,000/mm^3. *Phrenic Nerve Dysfunction* - presence of elevated dome of diaphragm with paradoxical motion on fluoroscopy or ultrasound. *Airway Problems* - bronchospasm, wheezing *Pleural Effusion* - fluid accumulation below the diaphragmatic surface of the lung causing blunting or obliteration of the costophrenic angle as seen on chest X ray. *Pulmonary congestion* - presence of vascular redistribution pattern of chest radiograph. *Pulmonary edema* - presence of bilateral alveolo-interstitial infiltrate on chest X ray not otherwise attributed to pneumonia. *Pneumothorax* - presence of air outside the visceral pleura of the lung as visualized on chest X ray. *Prolonged mechanical ventilation* - defined as those needing mechanical ventilation for more than 24 hours postoperatively. *Failed extubation* - defined as the need for reintubation within 48 hours of extubation.

Data Analysis. Data are expressed as mean. A one way analysis of variance followed by unpaired ***t*** test was utilized for comparison of groups 1 and 2. A $p < 0.05$ was considered statistically significant.

Results

A total of 107 patients were reviewed and included in the study. Ninety one patients (85%) were included in group 1 and whereas 16 patients (15%) were included in group 2. *Table I* shows the mean demographic and preoperative characteristics of patients in the two groups but there was no statistically significant difference noted between them. There are more females (n=73, 68%) than males (n=34, 32%) in the combined study population. The patients in group 2 (duration of postoperative mechanical ventilation < 24 hours) have lower FVC and FEV_1 but is not statistically significant. Both groups did not show preoperative hypoxemia nor hypercarbia. Other preoperative variables with statistical significance are left atrial and right ventricular size, ejection fraction and pulmonary artery pressure. There is also no statistical difference in terms of preoperative cardiac diagnosis and the valves involve as shown in *Table II*.

Table I. Mean Demographic and Preoperative Characteristics of 107 patients with Postoperative Mechanical Ventilation < 24 hours (group 1) vs > 24 hours (group 2).

Characteristics	Group 1 (n = 91)	Group 2 (n = 16)	p value
Age (years)	38.45 ± 9.7	39.8 ± 13.3	0.627
Sex			
Male	31	3	0.356
Female	60	13	
Weight (kgs)	52.14 ± 13.12	54.06 ± 14.48	0.596
Height (m)	1.59 ± 0.08	1.58 ± 0.05	0.729
BMI	20.63 ± 4.41	21.58 ± 5.62	0.449
Spirometry			
FVC	67.15 ± 14.50	56.33 ± 10.11	0.104
FEV_1	66.94 ± 14.01	54.50 ± 8.89	0.053
FEV_1/FVC	81.57 ± 7.74	82.50 ± 1.64	0.775
Arterial Blood Gas			
pH	7.31 ± 0.47	7.56 ± 0.51	0.137
pO_2	86.84 ± 7.91	84.66 ± 16.36	0.658
pCO_2	35.57 ± 3.20	34.16 ± 1.83	0.318
HCO_3	25.73 ± 2.23	27 ± 1.54	0.212
Creatinine	0.07 ± 0.02	0.08 ± 0.02	0.338
Echocardiography			
LA size (cms)	4.88 ± 0.71	4.68 ± 0.85	0.350
RV size (cms)	3.67 ± 0.45	3.60 ± 0.44	0.559
Number of valves affected	1.68 ± 0.82	1. 93 ± 0.25	0.258
Ejection Fraction	64 ± 6.66	61.31 ± 8.83	0.160
Pulmonary Artery Pressure (PAT)	59.71 ± 20.34	61.37 ± 21.93	0.766

Table II. Preoperative Cardiac Diagnosis

	Group 1 (n = 91)	Group 2 (n= 16)	p value
Rheumatic Heart Disease	85	16	0.58
Bicuspid Valve	1	0	1.00
Mitral Valve Prolapse	5	0	1.00
Mital Stenosis	76	11	0.17
Mitral Regurgitation	47	10	0.59
Aortic Stenosis	12	3	0.69
Aortic Regurgitation	22	2	0.51
Tricuspid Regurgitation	21	6	0.22

Intraoperative variables are shown in *Table III*. Patients in group 2 have significantly long duration of surgery with bypass time (*p=0.00001*) and ischemic time (*p=0.0002*) of 171.18 ± 65.84 minutes and 133.68 ± 53.78 minutes respectively against (133.68 ± 53.78 minutes and 94.39 ± 34.23 minutes in group 1. The number of packed RBC (*p=0.00000*) and fresh frozen plasma (*p=0.000227*) transfused is significantly greater in group 2 than in group 1. There is no statistically significant difference in number of platelets transfused (*p=0.391651*) in the two groups.

Table IV shows the postoperative complications noted in both groups. Six (37.5%) of 16 patients in group 2 developed pulmonary edema compared with four (4.3%) out of 91 patients in group 1 (*p=0.0006*). There are also significantly greater proportion of patients in group 2 who developed pleural effusion (11 or 68% in group 2 versus 16 or 17.5% in group 1), hospital acquired pneumonia (six or 37.5% in group 2 versus two or 2.1% in group 1) and unstable arrhythmia (four or 25% in group 2 versus none in group 1). Other complications that were noted but with no statistically significant difference are postoperative hemorrhage within 24 hours (*p=0.27*), atelectasis (*p=0.64*), pulmonary congestion (*p=0.22*) and sepsis (*p=0.27*).

Clinical outcome as measured by the number of days in the hospital and mortality are shown in *Table V*. Patients in group 1 have a significantly shorter total number of hospitalization (*p=0.003*) and postoperative hospital stay (*p=0.002*). One patient in group 2 died, for a mortality rate of 0.9%.

Discussion

In the present study of the duration of mechanical ventilation after cardiac valve surgery, 85% of patients were extubated in less than 24 hours postoperatively with no extubation failure reported, 14% were extubated within 24 to 72 hours postoperatively with one (0.9%) patient dead after 2 weeks due to severe sepsis. In earlier studies on post CABG patients, the incidence of PMV (>24 hours) was reported at 5.6% to 10.7%.[4] As of this time, there has been no study done in assessing the risk for PMV on homogenous patient population such as this. Several prediction models usually take the form of complex equations derived from logistic regression analysis[5-9] or of simplified additive scores where each variable is assigned a numeric ranking.[5,7,8] Most of these models included only the preoperative characteristics of the patient, however in most instances, the events in the intraoperative as well as the immediate post operative period contribute to postoperative complications. In this study, the variables investigated to probably affect the outcome of surgery included preoperative, intraoperative as well as immediate postoperative characteristics and events.

The preoperative assessment tools such as spirometry and arterial blood gases did not show correlation with occurrence of PMV in this study. FVC and FEV_1 showed a trend towards lower value for patients on group 2 but it did not reach statistically significant level. The value of routine preoperative pulmonary function testing remains controversial. Recent studies show that spirometry has a variable predictive value. In addition, clinical findings are generally more predictive of pulmonary complications rather than spirometric results in few studies that have evaluated both factors.[10-12] One potential reason for

Table III. Intraoperative Variables in Patients with Postoperative Mechanical Ventilation < 24 hrs (Group 1) and > 24 hours (Group 2).

Variable	Group 1 (n = 91)	Group 2 (n= 16)	p value
Bypass Time (minutes)	120.63 ±35.14	171.18±65.84	0.000010
Ischemic Time (minutes)	94.39 ± 34.23	133.68 ±53.78	0.000200
Number of Blood Unit Transfused			
Packed RBC	2.94 ± 1.53	5.37 ± 2.47	0.000001
Fresh Frozen Plasma	3.78 ± 2.92	7.75 ± 5.92	0.000227
Platelet Concentrate	4.84 ± 3.07	6.00 ± 3.70	0.391651

Table IV. Postoperative Complication in Patients with Postoperative Mechanical Ventilation < 24 hrs (Group 1) and > 24 hours (Group 2).

Variable	Group 1 (n = 91)	Group 2 (n= 16)	p value
Postoperative hemorrhage within 24 hrs	1	1	0.27
Atelectasis	8	2	0.64
Pulmonary Congestion	21	6	0.22
Pulmonary Edema	4	6	0.0006
Pleural Effusion	16	11	0.00007
Hospital Acquired Pneumonia	2	6	0.001
Unstable Arrhythmia	0	4	0.0003
Sepsis	1	1	0.27

Table V. Clinical Outcome in Patients with Postoperative Mechanical Ventilation < 24 hrs (Group 1) and > 24 hours (Group 2).

Variable	Group 1	Group 2	p value
Number of Days in the Hospital Postoperatively	10.02±5.2	14.92±9.4	0.003
Total number of Days in the Hospital	13.98±6.7	20.00±9.7	0.002
Mortality	0	1	-

preoperative pulmonary evaluation despite its poor correlation with outcome is to identify patients in whom the risk is so high that surgery should be canceled. However, even patients with very high risk as defined by spirometry can undergo surgery with an acceptable risk for pulmonary complications. Studies on PFT and high risk patients suggest that no threshold beyond which the risk of surgery is prohibitive.[13,14] Likewise, preoperative diagnosis and the number of valves involve did not predict the outcome.

Patients who smoke have a two-fold increased risk of postoperative complications even in the absence of COPD. The risk is highest in patients who smoked within the last 2 months.

Patients who quit smoking for more than 6 months have a risk similar to those who do not smoke. In some studies, complication rates almost reach the same level as that of non smoker after eight weeks of smoking cessation. In the result and data analysis, we did not included data on smoking history as we only had two patients in group 2 who smoked cigarette in the past.[15] The true significance of smoking history will not be seen in such a very small proportion of study population.

Several studies have shown that low BMI (<20 kg/min^2) as well as obesity (30 kg/min^2) were associated with increased duration of postoperative ventilation. In our study, patients have a mean BMI of 20 kg/min^2 and 21 kg/min^2 in group 1 and 2, respectively. There was no significant correlation noted in BMI with the outcome since most of these cardiac patients have low BMI and the number of our study population may not be enough to detect significant difference in this variable.

The duration of surgery had no bearing in the development of postoperative cardiac and pulmonary complications as reported in several earlier studies.[16] This is contrary to our study as we have noted that patients who received longer duration of postoperative ventilation had significantly longer duration of bypass time and ischemic time compared with patients in group 1. The number of packed RBC and plasma transfused intraoperatively also correlates well with the outcome.

In most studies, they reported atelectasis, pulmonary edema and pleural effusion as common complications following cardiac surgery.[17] In this study, we noted pulmonary congestion and pleural effusion as the most common postoperative pulmonary complication both occurring in 25.2% of study population. This is followed by atelectasis and pulmonary edema, both having an incidence of 9.3%. The postoperative pulmonary complications correlating well with prolonged mechanical ventilation are pulmonary edema, hospital acquired pneumonia, unstable arrhythmia and pleural effusion. These complication may have affected the postoperative course of the patient as reflected in the longer number of hospitalization days in patients with prolonged postoperative mechanical ventilation.

Conclusion

Preoperative factors are important predictors of patient's outcome after cardiac surgery a most studies have proven. However, in this study, preoperative variables did not correlate we with the outcome as measured by the duration of postoperative mechanical ventilation. The intraoperative events such as duration of surgery and number of blood units transfused during operation as well as immediate postoperative

complications such as unstable arrhythmia, pulmonary edema and pleural effusion are the factors that are strongly associated with prolonged mechanical ventilation.

Recommendation

We recommend further study on a large number of patients to formulate a scoring system that will include preoperative, intraoperative as well as immediate postoperative events to predict postoperative outcome.

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