Defining the Prevalence and Predictors of Restrictive and Obstructive Airway Pattern in a Non-Selected Malaysian Population

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ABSTRACT

Incidence of chronic obstructive pulmonary disease (COPD) is increasing in Malaysia. There is no reported study on spirometric airway obstruction, including restrictive and obstructive patterns, in the Malaysian population. This study was carried out to estimate the prevalence and predictors of airflow obstruction and conducted COPD symptom using the new AirSmart® Spirometry and COPD Population Screener (COPD-PS). The cross-sectional study was conducted in two tertiary hospitals using COPD-PS and AirSmart® Spirometry. There were 265 subjects recruited with 11% and 16% of the population respectively with restrictive and obstructive patterns. Twenty per cent of the subjects had COPD-PS score more than five. Seventy-four per cent of subjects with obstructive active or past smokers (p=0.03, p<0.01), while subjects with restrictive pattern were more likely to have body mass index (BMI) of more than 23 (or 2.52, 95% CI: 1.02-5.62) (p<0.01). There was a negative correlation between "forced vital capacity" and BMI (r=-0.5813, p<0.001). This study reported the high prevalence of airflow obstruction including restrictive pattern using the new AirSmart® Spirometer. Un-diagnosed COPD and high BMI may contribute to airflow obstruction in our population.

Keywords: COPD, obesity, obstructive airway
ABSTRACT

The incidence of chronic obstructive pulmonary disease (COPD) in Malaysia appears to be increasing. To date, there are no local studies describing restrictive and obstructive airflow limitation patterns using spirometry. We conducted a cross-sectional study to determine the prevalence and predictors of airflow limitation symptoms by screening for COPD symptoms with the COPD Population Screener (COPD-PS) questionnaire and determined the airflow limitation using the new hand-held device, AirSmart®. We recruited 265 subjects. Eleven percent had restrictive pattern and 16% had obstructive pattern. Twenty percent of subjects had COPD-PS score of more than five. In the obstructive pattern group, 74% were active or ex-smokers (p=0.03, p<0.01), whilst those with restrictive pattern were more likely to be heavier with a body mass index (BMI) of more than 23 (OR 2.52, 95% CI: 1.02-5.62) (p<0.01). There was a negative correlation between forced vital capacity and BMI (r=-0.5813, p<0.001). We found a high prevalence restrictive pattern of airflow limitation using the new AirSmart® Spirometer. There appeared to be a large proportion of undiagnosed obstructive airway diseases and higher BMI could be the causes of limitation of airflow in our subjects.

Keywords: airflow limitation, COPD, obesity

INTRODUCTION

In 2017, chronic obstructive pulmonary disease (COPD) was reported to be the 6th most common cause of death in Malaysia (8 Global Burden of Diseases (GBD) profile: Malaysia 2017). A suburban Malaysian population study reported 6.5% prevalence of COPD whilst a study in selected Malaysian primary health care centres found a similar (6%) prevalence of airflow obstruction (Loh et al. 2016; Sui et al. 2015).

Due to the low cost of office-based spirometry devices, detecting COPD by screening asymptomatic individuals could be performed. Many guidelines advocate against screening for COPD in subjects with no symptoms. The US Preventive Services Task Force (USPSTF) have deemed it showed minimal benefit and lacked cost effectiveness (Force et al. 2016; Guirguis-Blake et al. 2016). Most studies select high-risk subjects based on their risk factors such as the presence of a smoking history. (Stanley et al. 2014; Yawn et al. 2014). Most of these studies were performed in primary care-based population in North America and Europe.

There is still paucity of local data on airflow limitation including restrictive pattern among the Malaysian population. Previous unpublished data from the Malaysian Thoracic Society have highlighted an increased prevalence of restrictive pattern in previous screening programmes.
More recently studies have shown that a restrictive spirometric pattern is relatively common and associated with co-morbidities such as cardiovascular diseases, diabetes, stroke and hypertension (Guerra et al. 2010; Kurth & Hnizdo 2015; Mannino et al. 2003). Population based studies also suggest that a relationship between restrictive pattern on spirometry and a higher body mass index (BMI) and decreased lung volume is associated with an increased adipose tissue in the central body region (Mannino et al. 2012). With obesity on the rise in Malaysia (Suzana et al. 2012), this is the first study to measure the prevalence of spirometric restrictive pattern as a potential respiratory implication of the rising obesity pandemic.

This study was conducted to estimate the prevalence and predictors of airflow limitation (obstructive and restrictive patterns) and screen for COPD symptoms using both the COPD-PS questionnaire and the handheld spirometry device AirSmart® Spirometer (Pond Healthcare, Sweden).

MATERIALS AND METHODS

Study Population

This was a cross-sectional study to determine the prevalence of airflow limitation and undiagnosed COPD subjects using a validated 5-item questionnaire (COPD-PS) and the new AirSmart® Spirometry device. A sample size of 224 was calculated using estimation for single proportion to determine the prevalence of airflow limitation. Convenience sampling was performed in two tertiary medical institutions (Universiti Kebangsaan Malaysia Medical Centre (UKMMC) and Universiti Technologi Mara, Hospital Selayang Campus) during the World COPD programme. This programme launched a one-day official screening programme including educational seminars on chronic lung diseases, smoking and electronic cigarettes. Ethical approval was obtained from the hospital’s ethical board.

Only participants above 21 years with no history of medical diagnosis of respiratory disease, were included. Those with pregnancy, moderate to severe cognitive impairment and/or a within three-month history of myocardial infarction, cerebrovascular event and pneumothorax, were excluded.

Data Collection

Subject demographics (age, smoking history, health status, BMI) and the validated COPD Population Screener™ (COPD-PS, Quality Metric Incorporated, Lincoln, Rode Island, USA) were filled during a physician-led consultation process. The COPD-PS is a validated 5-item questionnaire, with a high accurate classification rate to detect airflow obstruction. It has a good balance between sensitivity and specificity. It is self-administered, simple and short. It has been be both reliable and valid (AUC=0.89 compared to physician-reported COPD) (Stanley et al. 2014). A score of 5 and more had high probability to suffer from COPD. Of particular interest was that the questionnaire was
developed specifically for the general population and not subjects who have respiratory symptoms (Force et al. 2016; Stanley et al. 2014).

Subjects then performed a forced expiratory volume using the AirSmart® Spirometer (Pond Healthcare, Sweden). The tests were conducted by respiratory technicians with formal spirometry training which was standardised again before convenience sampling. The AirSmart® Spirometer is a handheld spirometer device that connects to the Air Smart® Spirometer application from the App Store that could be used with any i-devices. A disposable, single-used FlowMir® turbine was used for each subject. The spirometer did not require calibration for each subject or on each day of data collection. Subjects were asked to blow out for 6 seconds according to the American Thoracic Society (ATS) criteria. This was performed at least three times and a maximum up to five tests, depending on the quality of the tests. A minimum of three acceptable measurements were recorded for each subject; and the test will only be considered if the variation between the two best readings was <5%. Once these manoeuvres were performed, the final results would be displayed, including forced expiratory volume in 1 second (FEV1), forced vital capacity (FVC) and FEV1/FVC ratio. As there had been no recent study examining the general Malaysian population, spirometric reference values were based on the study by Hankinson et al. (1999), as proposed by the Centers for Disease Control and Prevention in the United States. Bronchodilation was not performed in this study.

The final results displayed in the application were the best value obtained after performing the desired number of tests. The spirometric results were interpreted by a respiratory physician in which any abnormality reported would lead to an on-site physician-led counselling. Subjects who may have undiagnosed COPD were categorised according to the Global Initiative for Chronic Obstructive Lung Disease (GOLD) guidelines based on their FEV1 percentage, and their FEV1/FVC ratio of <0.7. Any abnormalities in the test including a low FEV1 and FVC of <80%, with reduced or increased FEV1/FVC were categorised as restrictive and obstructive patterns, respectively. These subjects were subjected to counselling and referred for formal spirometry testing, chest radiograph (CXR) and respiratory clinic follow-up. All data are presented as a mean with standard deviation (SD).

**Statistical Analysis**

GraphPad Prism 7 (GraphPad Software, Inc, California) and SPSS statistical software version 21 (SPSS, IBM, Armonk, New York, USA) were used for analysis. The Chi-Square and independent t-test were used for categorical and continuous variables comparing two groups while multiple logistic regression analysis was used to search for predictors of subject with airflow limitation. The Pearson correlation coefficient test was performed for BMI and FVC for identified restrictive airway patterns on spirometry. All analyses were
performed with 95% confidence intervals (CI) and the level of significance was set at p-value of less than 0.05.

### RESULTS

A total of 265 subjects were recruited from two hospitals which concomitantly organised a screening programme to detect both airflow limitation and COPD in a non-pre-selected population. Subject demographics and smoking history in the two hospitals are shown in Table 1.

Out of 265 subjects, 29 (10.9%) had restrictive pattern on their spirometry while 42 (15.8%) had obstructive...
pattern. The remainder 194 subjects (73.2%) had normal spirometry. Among the restrictive spirometry group, 24 (83%) of the subjects were females. However, 29 (69%) with obstructive pattern were males. The majority of subjects, i.e. 29 (90%) with restrictive pattern were non-smokers (p<0.01). On the other hand, the majority of subjects, i.e. 31 (74%) who had an obstructive pattern were either active or ex-smokers (p=0.03, p<0.01). There were also differences in the mean BMI (SD) in which the restrictive pattern group 25.1 (6.7) was significantly higher than the obstructive group 23.5 (2.5) (p=0.03). There were no statistically significant differences in FEV1 between the two groups however, the mean FVC (SD) was significantly lower in the restrictive group, 2.26 (0.91) vs 2.76 (0.49) (p=0.03).
Fifty-four (20.3%) out of the 265 subjects had COPD-PS score of five or more. Thirty-five (65%) of these subjects had obstructive pattern. Only one subject (2%) out of 54 with COPD-PS score of more than five never smoked while the rest were either active smokers or ex-smokers. Previous exposure to biomass was reported in two subjects (4%) out of 54. The baseline mean FEV1 (SD) and the FEV1/FVC ratio were significantly lower in subjects with COPD-PS of more than five compared to those with scores of less than five (Table 2).

Using the multiple logistic regression adjusted to all the variables in the model, age more than 55 were more likely to have either obstructive (OR 2.3, 95% CI: 1.74-32.12) (p<0.001) or restrictive (OR 1.89, 95% CI: 0.98-2.12) (p<0.01) patterns compared to younger subjects (Table 3). Subjects with respiratory complains such as shortness of breath and had a total score of COPD-PS >5 were more likely to have an obstructive pattern. Subjects with BMI of more than 23 were more likely to have a restrictive pattern (OR 2.52, 95% CI: 1.05-5.62) (p<0.01). There was a negative correlation between FVC and BMI (rs=-0.5813, p<0.001) (Figure 1).

![Figure 1: Association between FVC and BMI using the Spearman correlation analysis](image-url)
Table 4 shows the percentage of subjects who returned for formal assessment. Despite counselling and referral for all subjects with restrictive and obstructive patterns for formal spirometry, CXR and clinic follow-up, only 17 and 21% of subjects with restrictive and obstructive patterns, respectively, returned for formal spirometry in which the majority of these subjects also had a chest radiograph and attended clinic. A final diagnosis of idiopathic pulmonary fibrosis was diagnosed for one restrictive pattern based on clinical parameters and chest radiograph findings. Three final diagnosis of COPD were diagnosed on subjects who presented back with obstructive patterns, leading to two that were commenced on treatment and a smoking cessation clinic referral.

The six subjects that were not diagnosed with COPD but had obstructive pattern on AirSmart® spirometry reported no symptoms nor reversibility post-bronchodilatation on their formal spirometry based on the ATS/ERS Task Force to suggest asthma or asthma-COPD overlap (Miller et al. 2005). One subject was referred for impulse oscillometry which was normal. None of these six subjects were commenced on medications.

DISCUSSION

The percentage of airflow obstruction has been reported from 3-15% while restrictive pattern ranges from 1-7% in the Western population (Force et al. 2016; Guirguis-Blake et al. 2016; Stanley et al. 2014; Yawn et al. 2014). However, prevalent studies in Asia are lacking. For example, a Korean study found undiagnosed airflow obstruction present in 3.5% of women and more (12.4%) in men (Kim et al. 2005). There are very few spirometric studies in Malaysia in which the largest study with 1,999 subjects dated back in 1993. However, this study reported only absolute mean values of FVC and FEV1 in males only, which were reported to be lower than the observed mean in other Western studies (Singh et al. 1993). This study did not look at the prevalence of airflow limitation which included both obstructive and restrictive patterns.

One screening study of 83 participants in Malaysia reported 15.7% prevalence of undiagnosed COPD using the COPD-PS questionnaire and Vitalograph hand-held spirometry device (Sui et al. 2015). Another study with 416 subjects reported a prevalence of airflow limitation in
10.6%, using the Vitalograph as well (Ching et al. 2014). However, this study only assessed subjects who were more than 40 years old with more than 10 pack-years smoking history. Another recent Malaysian population-based epidemiology data on COPD estimated a 6.5% prevalence of COPD. Interestingly, our study detected higher prevalence of obstructive airway pattern which might be also due to undiagnosed asthma as the population screened was not specifically targeted for COPD. The heterogeneity of the population examined might explain the discordancy between these studies. Further and larger epidemiological studies are required to ascertain this prevalence for certain. However, our study reports for the first time a high prevalence of restrictive as well as obstructive lung patterns in asymptomatic subjects in Malaysia.

Spirometry testing in Malaysia are still costly and can cost up to USD 250 in the private sector while the AirSmart® Spirometer only cost USD 20 which is makes it affordable to both general practitioners or community pharmacies. The AirSmart® device is created to deliver a superior user experience at the lowest cost possible compared to other hand-held devices such as the Vitalograph. The need for repeat calibration is the other disadvantage of other hand-held devices compared to the AirSmart® device. This was the first study to report the feasibility of using the AirSmart Spirometer® in detecting airflow limitation in a non-preselected population in Malaysia. We observed restrictive and obstructive patterns in 11% and 16% of the screened population, respectively, which were higher than expected. Smokers or ex-smokers comprised the majority of subjects with obstructive patterns on their spirometry. These findings suggest a higher degree of under-recognition of airflow limitation which might include COPD.

Twenty percent of the population screened had COPD-PS score of more than five which highlights a high prevalence of respiratory symptoms in this screened population. However, the sensitivity and specificity of the COPD-PS questionnaire has not been tested in an urban, Asian population. Meta-analysis has reported that hand-held flow meters supervised by trained health professionals proved more accurate than questionnaires in discriminating smokers with and without airway obstruction (Haroon et al. 2015).

The high prevalence of undiagnosed COPD (10-20%) and population detected screening with a simple non-invasive test such as questionnaires and spirometry have led to the argument that screening for COPD could be justified (Force et al. 2016; Guirguis-Blake et al. 2016). On the other hand, concerns about subject-centred benefits in mild asymptomatic subjects with high monthly costs of inhalers may render screening not cost-effective. Recently, the US Preventive Services Task Force (USPSTF) recommends against screening for COPD in asymptomatic individuals (Force et al. 2016; Guirguis-Blake et al. 2016). The recommendation is based on a review which showed lack
of evidence of benefits screening for COPD in asymptomatic adults for COPD using questionnaires or office-based screening pulmonary function test (Guirguis-Blake et al. 2016). There are also lack of data supporting the treatment benefits in screen-detected populations. There are however some data suggesting a benefit of combining both questionnaires and pulmonary function test which may improve the accuracy of the tests (Haroon et al. 2015). To date, there are no epidemiology studies done comparing active screening with no screening to determine whether primary care screening for COPD improves health outcomes including cost-effectiveness.

There are no treatment trials which have been performed in screened populations. However, trials and sub-analyses in population with mild-to-moderate symptomatic COPD individuals have shown a small reduction in COPD exacerbation frequency. Epidemiologic studies with in the same COPD group have reported an average of less than one exacerbation per year, and it is intuitively expected that subjects with screen-detected COPD might be expected to have even fewer exacerbations (Vogelmeier et al. 2017). As accelerated FEV1 decline is observed especially in moderate (Stage 2) COPD, Zhou et al. (2017) recently reported that early intervention with bronchodilator ameliorate the decline of FEV1 in Stage 1 and 2 COPD. However, as cost-effective analysis on early intervention for COPD is lacking; further studies are required to elucidate further the role of screening for asymptomatic early stage COPD. This study observed that the default rate for follow-up for asymptomatic subjects was high which might not justify screening. Nevertheless, there might be a basis to screen for symptomatic early stage COPD as active smoking, physical limitations and shortness of breath have been associated with further FEV1 decline and risk for exacerbations, in which subjects could benefit from early intervention (Chen et al. 2017; Ekberg-Aronsson et al. 2005).

In this study, despite high prevalence of airflow limitation on screening, a very small percentage of subjects return for formal assessment which may suggest that screening in mildly or asymptomatic subjects are not cost-effective, in line with the US Preventive Services Task Force (USPSTF) (2016) recommendation. Although this is not a number needed to treat (NNT) study, three COPD final diagnoses were made despite only 20% of subjects returning for formal assessment with formal spirometry, CXR and respiratory clinic referral. Two of these subjects were diagnosed with COPD stage III or IV. This led to commencement of treatment for both subjects and one smoking cessation clinic referral.

In six subjects who returned for assessment but were not diagnosed with COPD, no other diagnosis such as asthma or bronchiectasis were made to have led to the commencement of specific treatment. Although there is not sufficient data to infer the cause for this, we speculate these subjects who were otherwise healthy returned for formal assessment due to increased health awareness and reduced health
risk behaviour without an underlying respiratory problems. Therefore, this may enhance a health-seeking behaviour after being initially informed that their spirometry was abnormal. This study also highlights that despite counselling, only a small percentage of subjects subsequently returned for formal assessments. Although this could not be generalised specifically to different population, this further highlights at very best the modest benefit of screening asymptomatic or mildly symptomatic subjects. Most studies on COPD screening failed to show acceptability and uptake of these tests and this is important to consider for overall effectiveness (Force et al. 2016; Guirguis-Blake et al. 2016; Stanley et al. 2014).

COPD screening has shown potential benefit in the increase of smoking cessation rates and the reduction of progress from mild to moderate COPD (Scanlon et al. 2000). One study reported a significant increase in biochemically confirmed cessation rate of 7% when screening was performed with NNT=14 (Parkes et al. 2008). Further studies are required to determine if COPD screening indeed leads to increase awareness of COPD diagnosis and increased smoking cessation rates. In this study, despite poor compliance for subsequent formal assessment, one subject was referred for smoking cessation and is currently reported to actively attend the smoking cessation clinic.

This study also reported for the first time the high prevalence of restrictive pattern via spirometry testing in a Malaysian population. In contrast to obstructive patterns, restrictive pattern was associated with females, non-smokers and BMI. However, as reduced total lung capacity or slow vital capacity could not be interpreted using this hand-held device, the disease criteria of fixed-ratio used for classifying a restrictive pattern on spirometry with FVC <80% predicted and FEV1/FVC ratio >80% might not accurately estimate the prevalence of restrictive pattern in this population.

High BMI significantly and negatively correlate with FVC. It is reported that 18% of the country are classified as obese whilst a further 30% are overweight (Mohamud et al. 2011). Although respiratory symptoms were not strongly associated with restrictive patterns, this study indicates that Malaysia is facing an obesity endemic which could also impact respiratory function. Restrictive pattern on spirometry is associated with increased incidence and mortality from diabetes, stroke, cardiovascular disease, hypertension (Guerra et al. 2010; Kurth & Hnizdo 2015; Mannino et al. 2003).

We had few limitations in our study. This was a cross-sectional method and the variables do not determine absolute causality and predictors could not be accurately validated compared to a cohort study. This study involved a small number of participants based on a population screened in two hospitals and therefore its application to the general public must be taken in caution. However, the lack of spirometric and COPD screening studies in Malaysia render this report an important initial observation for
CONCLUSION

In this study, we report a high prevalence of airflow limitation including restrictive and obstructive patterns using the new AirSmart® Spirometer. Although COPD screening has not been recommended due to lack of evidence from a cost-effectiveness and clinical benefits impact, this study highlights that screening for airflow limitation due to possible causes such as COPD and/or high BMI using simple tools such as hand-held devices and a COPD screening questionnaire is feasible.

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