ORIGINAL RESEARCH

ASSESSMENT OF RATIO OF PEAK EXPIRATORY FLOW RATE TO VITAL CAPACITY FOR IDENTIFYING PULMONARY FIBROSIS

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ABSTRACT

Background: Pulmonary fibrosis (PF) is associated with reduction in vital capacity (VC) and increase in expiratory flow rates, including peak expiratory flow (PEF). Full pulmonary function testing and computed tomography chest scans are limited resources in some geographic areas and a simple and sensitive screening test would be of value. We hypothesized that increase in the ratio of % predicted PEF over % predicted VC (%PEF/%VC), from spirometry alone might be sensitive to screen for pulmonary fibrosis.

Methods: The %PEF/%VC from 1,000 consecutive spirometric flow volume curves was nearly normally distributed: 7.5% (approximately 1.5 standard deviations) had a ratio ≥ 1.4 . We evaluated the sensitivity and specificity of this cut point for a diagnosis of PF in a retrospective chart review of 391 patients with good quality spirometry and respirologists' confirmed diagnoses.

Results: Of the 391 patients analyzed, 98 had PF, 79 were normal, 70 had a combined obstructive and restrictive processes, 57 had obstructive lung disease, 61 had extra-parenchymal restriction and 26 had non-fibrotic interstitial lung disease. A %PEF/%VC ≥ 1.4 was only 54.1% sensitive in predicting PF, however it had a specificity of 94.9%. There was a 95.1% specificity for ruling in intra-parenchymal opposed to extra-parenchymal restriction.

Conclusion: A %PEF/%VC ≥ 1.4 was not sensitive enough to screen for PF but did demonstrate high specificity and thus may be helpful in identifying intraparenchymal restriction.

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INTRODUCTION

Pulmonary fibrosis is a group of conditions associated with parenchymal scarring and subsequent restrictive lung disease [1]. A reduction in vital capacity (VC) is the primary functional index which identifies restrictive changes in parenchymal fibrosis and a reduced VC can occur in not only intra-parenchymal but also extra-parenchymal processes [2]. Computed tomography (CT) chest, the major diagnostic investigation in interstitial pulmonary fibrosis, is associated with radiation exposure. In addition, CT scans, lung volumes and diffusion capacity are limited resources that cannot be performed in many rural or remote centres. Spirometry alone is a simple test that is accessible in many clinics. A sensitive test using peak expiratory flow (PEF) and slow VC, measured from a low volume curve, could be a useful screening tool to identify patients with parenchymal scarring.

Peak expiratory flow is obtained from flow-volume curve data. It is the maximum expiratory flow achieved from a maximum forced expiration [3]. Peak expiratory flow has been used in the assessment of control in asthma patients but has not been studied in the assessment of parenchymal scarring [4]. Due to the scarring of the surrounding parenchyma, radial traction prevents dynamic compression of the airways and subsequently increases all force expiratory flow rates, including PEF [5]. In addition, increased elastance of the parenchyma contributes to an increase in recoil, also causing an increase in flow rates.

A decline in VC in pulmonary fibrosis is due to reduced lung compliance and its measurement is recommended in current guidelines as, over time, its value reliably predicts mortality in patients with idiopathic pulmonary fibrosis [6].

A simple routinely available highly sensitive screening test would be of value particularly in geographical areas with limited access to sophisticated pulmonary function testing and high resolution CT scanning. Since PEF is increased and VC is decreased in pulmonary fibrosis, we reasoned that a ratio comprised of percent predicted PEF over percent predicted vital capacity (%PEF/%VC) would be elevated in this condition and we hypothesized that an elevated ratio would be a diagnostically sensitive test with a consequent high negative predictive value. We also examined this index in its ability to differentiate intra-parenchymal versus extra-parenchymal causes of restriction.

METHODS

Initially, 1,000 consecutive and unselected flow volume values from a tertiary care community pulmonary function laboratory (Royal University Hospital, Saskatoon, SK) were analysed to evaluate the distribution of %PEF/%VC in the population. The percent predicted pre-bronchodilator PEF (%PEF) and slow VC (%VC) were utilized. A near normal distribution was demonstrated with 7.5% (approximately 1.5 standard deviations) of the population having a %PEF/%VC ratio ≥ 1.4 (data available on request). A subsequent retrospective chart review was performed on 391 patients with good quality spirometry, pulmonary imaging and respirologists' confirmed diagnoses. The study was approved by the University of Saskatchewan Biomedical Research Ethics Board, permit number 17-308.

Data were extracted from the flow volume curves performed using the Vmax[®] computerized pulmonary function system (Viasys Healthcare Inc., Conshohocken, PA). From the respirologists' notes and chest image findings, patients were sorted into the following categories for analysis: pulmonary fibrosis; normal; obstructive lung disease; extra-parenchymal restriction; other (non-fibrotic interstitial lung disease, ILD, etc.); and combined obstructive and restrictive processes. Data, including

gender, body mass index (BMI), age and diagnosis, were documented. Patients without good quality pulmonary function testing as per American Thoracic Society criteria [7] or chest imaging were excluded.

The PEF ratio was calculated for each patient and analyzed as per their diagnostic subgroup. The sensitivity and specificity of the %PEF/%VC ≥ 1.4 for predicting pulmonary fibrosis in all-comers was calculated. The specificity of the PEF ratio ≥ 1.4 in identifying pulmonary fibrosis in all restrictive lung disease was also identified.

A receiver operator characteristic (ROC) curve was created to assess the diagnostic and predictive accuracy of the PEF ratio and to identify the most appropriate cut-off to maximize both sensitivity and specificity.

RESULTS

A total of 391 patients were included in the study. Of these patients, 198 were male, 193 were female, the mean age was 63.2 years and the mean BMI was 28.3 kg/m². Patients' imaging and respirology consultation were reviewed and they were subsequently categorized according to diagnosis: 79 patients were normal, the majority having chronic cough related to non-pulmonary causes such as upper airway cough syndrome; 98 had pulmonary fibrosis; 26 had non-fibrotic ILD such as non-fibrotic non-specific interstitial pneumonia and organizing pneumonia; 57 had isolated obstructive lung disease (mostly chronic obstructive pulmonary disease, COPD, or asthma); and 61 had extra-parenchymal restrictive lung disease (obesity (n=53), chest wall deformity (n=3), pleural disease (n=2) and neuromuscular disease (n=3)). Combined obstructive and restrictive disease was identified in 70 patients with the majority having COPD with pulmonary fibrosis (n=37) and COPD with obesity (n=23).

The PEF ratio was calculated for all patients and analyzed as per their diagnosis (Table 1). The mean %PEF/%VC ratio in patients with pulmonary fibrosis

TABLE 1.
BASELINE PATIENT CHARACTERISTICS IN THE TOTAL POPULATION AND BY TUMOUR INFILTRATING LYMPHOCYTE EXPRESSION.

Diagnosis	Number of patients* (N=391)	%PEF/%VC ≥ 1.4 n (%)	%PEF/%VC mean (SD)	p value (compared with PF)
Pulmonary fibrosis	98	53 (54%)	1.48(0.43)	-
Normal	79	1 (1.3%)	0.95(0.18)	<0.00001
Combined obstruction and restriction	70	5 (7.1%)	0.97(0.30)	<0.00001
Obstructive pulmonary disease	57	0	0.70(0.22)	<0.00001
Extra-parenchymal restriction	61	3 (4.9%)	1.04(0.24)	0.002
Non-fibrotic ILD	26	6 (19%)	1.18(0.32)	<0.00001

Abbreviations: HPF, high power field; M, presence of distant metastasis; N, lymph node involvement; T, primary tumour site; TNM, tumour, node, metastasis

was 1.48, which was significantly higher ($p=0.002$ to $p<0.0001$) than those who were normal (ratio=0.95), who had combined obstructive and restrictive physiology (ratio=0.97), obstruction (ratio=0.70), those with extra-parenchymal restriction (ratio=1.04) or those with non-fibrotic ILD (ratio=1.18).

The sensitivity of the PEF ratio in predicting pulmonary fibrosis in this population was poor at 54.1%. This is demonstrated visually with the scatter plot in Figure 1. However, the specificity of the PEF ratio ≥ 1.4 was high at 94.9%. The specificity of the %PEF/%VC ratio ≥ 1.4 in differentiating pulmonary fibrosis in all causes of restrictive lung disease was 95.1%. Utilizing a ratio of 1.3 proved to be more sensitive (61%) with minimal reduction in specificity (91%) (ROC curve data available on request).

FIGURE 1.
INDIVIDUAL PEAK EXPIRATORY FLOW RATIO
IN 98 PATIENTS WITH PULMONARY FIBROSIS.

DISCUSSION

The PEF ratio was not sensitive for identifying pulmonary fibrosis in this population. This ratio would, therefore, not be a useful screening test as initially hypothesized. However, the specificity of %PEF/%VC ratio ≥ 1.4 was high and therefore may be useful, when < 1.4 , in identifying those patients without pulmonary fibrosis. Also given that the specificity was excellent in identifying those with intra-parenchymal versus extra-parenchymal causes of restriction which may be valuable.

The test itself utilizes only the spirometric techniques of PEF and slow VC and can, therefore, be advantageous in geographical settings (e.g., developing countries and rural areas, where spirometry is available but where full pulmonary function testing and CT chest may be of limited availability). Computed tomography

is also associated with the additional risk of significant radiation exposure.

Limitations of the study include the difficulty in proper assessment of PEF, which should be achieved with a sharp rise and occur close to the point of maximal inflation but is often subject-dependent. Coughing, spitting and blocking the mouthpiece with one's tongue may falsely elevate the PEF [3]. In a primary care setting, full expiration during slow VC may not be achieved, depending on operator technique and comfortability with the test, and this may also falsely elevate the PEF ratio. Relatively few patients with neuromuscular disease were evaluated in this study; however, it is predicted that their PEF may be reduced due to muscular weakness and may still yield a PEF ratio less than 1.4. This hypothesis would require further analysis for confirmation.

CONCLUSION

The PEF ratio was not sensitive enough to be of major value as a screening test for pulmonary fibrosis, but did demonstrate high specificity and may be helpful in identifying intraparenchymal restriction.

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