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A new spirometry-based algorithm to predict occupational pulmonary restrictive impairment

S. De Matteis[1], A. A. Iridoy-Zulet[2], S. Aaron[3], A. Swann[4] and P. Cullinan[1]

[1]Department of Respiratory Epidemiology, Occupational Medicine and Public Health, Imperial College London, London SW3 6LR, UK, [2]Respiratory Unit, Navarra Hospital Complex, Pamplona 31008, Spain, [3]Department of Respiratory Medicine, The Ottawa Hospital, Ottawa, Ontario K1H 8L6, Canada, [4]Occupational Health Service, Imperial College London, London SW7 2AZ, UK.

Correspondence to: S. De Matteis, Department of Respiratory Epidemiology, Occupational Medicine and Public Health, National Heart and Lung Institute, Imperial College London, Emmanuel Kaye Building, 1b Manresa Road, London SW3 6LR, UK. Tel: +44 (0)20 759 43177; fax: +44 (0)20 7351 8336; e-mail: s.de-matteis@imperial.ac.uk

Background Spirometry is often included in workplace-based respiratory surveillance programmes but its performance in the identification of restrictive lung disease is poor, especially when the prevalence of this condition is low in the tested population.

Aims To improve the specificity (Sp) and positive predictive value (PPV) of current spirometry-based algorithms in the diagnosis of restrictive pulmonary impairment in the workplace and to reduce the proportion of false positives findings and, as a result, unnecessary referrals for lung volume measurements.

Methods We re-analysed two studies of hospital patients, respectively used to derive and validate a recommended spirometry-based algorithm [forced vital capacity (FVC) < 85% predicted and forced expiratory volume in 1 s (FEV1)/FVC > 55%] for the recognition of restrictive pulmonary impairment. We used true lung restrictive cases as a reference standard in 2 × 2 contingency tables to estimate sensitivity (Sn), Sp and PPV and negative predictive values for each diagnostic cut-off. We simulated a working population aged <65 years and with a disease prevalence ranging 1–10% and compared our best algorithm with those previously reported using receiver operating characteristic curves.

Results There were 376 patients available from the two studies for inclusion. Our best algorithm (FVC < 70% predicted and FEV1/FVC ≥ 70%) achieved the highest Sp (96%) and PPV (67 and 15% for a disease prevalence of 10 and 1%, respectively) with the lowest proportion of false positives (4%); its high Sn (71%) predicted the highest proportion of correctly classified restrictive cases (91%).

Conclusions Our new spirometry-based algorithm may be adopted to accurately exclude pulmonary restriction and to possibly reduce unnecessary lung volume testing in an occupational health setting.

Key words Diagnostic algorithm; occupational health; restrictive lung pattern; spirometry.

Introduction

Spirometry is frequently used in occupational health surveillance to detect both 'obstructive' and 'restrictive' pulmonary impairment but its performance in diagnosing restrictive lung diseases is generally poor. Current guidance on the interpretation of spirometric measurements [1] in relation to pulmonary restriction makes reference to an algorithm [2] designed to have a very high sensitivity (Sn) so that it can be applied safely in primary care to minimize the risk of a false negative test; the cost is a relatively high proportion of false positive tests. This may be inappropriate in an occupational health setting where the expected prevalence of restrictive lung disease is *a priori* low (at most 1–10%) and access to confirmatory measurements of lung volume in hospital-based departments of respiratory physiology is generally difficult.

We set out to explore the specificity (Sp) and the positive predictive value (PPV) of current spirometry-based algorithms and compare their efficiency in the detection of restrictive pulmonary impairment in low-prevalence settings.

Methods

We re-analysed two previous studies of 259 and 265 patients, respectively used to derive and validate a current, standard spirometry-based algorithm [forced vital capacity (FVC) < 85% predicted and forced expiratory volume in 1 s (FEV_1)/FVC > 55%] used to identify restrictive pulmonary impairment. Details of the study have been previously described [2]; the patients were White adults consecutively referred by their physician for both spirometry and lung volumes tests at the Ottawa Hospital in Ontario, Canada between 2000 and 2001. Each patient underwent standardized spirometry and, subsequently, a measurement of total lung capacity (TLC) by plethysmography. Written informed consent for all the study subjects and ethical approval was previously reported [2]. We considered a TLC below the predicted lower limit of normal as a reference standard for true lung restriction and used 2 × 2 contingency tables to estimate the Sn, Sp and PPV and negative predictive values with corresponding 95% confidence intervals for a series of spirometric algorithms.

Because our population of interest is active workers, we tested the performance of each diagnostic algorithm in subjects under the age of 65 years and with simulated low prevalences of restrictive disease (10 and 1%). We evaluated multiple diagnostic cut-points of FVC and FEV_1/FVC ratio to maximize Sp (target ≥ 94%) and so PPV in order to minimize the false positive rate and compared the performance of our best diagnostic algorithm with those previously reported [2–5] by using receiver operating characteristic (ROC) curves. We did not test algorithms whose performance was comparable to the standard one [2] and/or computationally more intense and/or more difficult to interpret in routine clinical practice [6]. In addition, we compared predicted values for spirometry parameters using both Crapo [7] and Hankinson [8] reference equations. Finally, the best algorithm generated in the derivation data set was applied to the validation data set, and its performance was re-assessed.

Table 1. Comparison of selected previous diagnostic algorithms versus ours using Hankinson prediction equations among adults aged under 65 years (*n* = 186)

Diagnostic algorithm	Restricted lung disease						
	Yes (*n*)	No (*n*)	Prev. (%)	PPV (%)	95% CI	NPV (%)	95% CI
This study (2015)							
FVC < 70%p + FEV_1/FVC ≥ 70%							
Yes (*n*)	24	**6**					
No (*n*)	10	146					
Sn (95% CI)	71	53–85	10	67	47–82	97	95–98
Sp (95% CI)	96	92–99	1	15	7–29	100	99–100
Glady *et al.* [2]							
FVC < 85%p + FEV_1/FVC ≥ 55%							
Yes (*n*)	33	**64**					
No (*n*)	1	88					
Sn (95% CI)	97	85–100	10	20	17–24	99	96–100
Sp (95% CI)	58	50–66	1	2	2–3	100	99–100
Khalid *et al.* [3]							
[(FEV_1/FVC)%p/FVC%p] ≥ 1.11							
Yes (*n*)	33	**74**					
No (*n*)	78	1					
Sn (95% CI)	97	85–100	10	18	16–21	99	96–100
Sp (95% CI)	51	43–60	1	2	1–2	100	99–100
Mehrparvar *et al.* [4]							
FVC < LLN + FEV1/FVC ≥ LLN							
Yes (*n*)	27	**34**					
No (*n*)	7	118					
Sn (95% CI)	79	62–91	10	28	22–36	97	95–99
Sp (95% CI)	78	70–84	1	3	2–5	100	99–100
Venkateshiah *et al.* [5]							
FVC < LLN							
Yes (*n*)	33	**56**					
No (*n*)	1	96					
Sn (95% CI)	97	85–100	10	23	19–27	99	97–100
Sp (95% CI)	63	55–71	1	3	2–3	100	99–100

n, number; p, predicted; Prev., prevalence of restrictive disease; LLN, lower limit of normal; NPV, negative predictive values; 95% CI, confidence interval. Percentages are rounded up. Values in bold: number of false positives.

Statistical analyses were undertaken using Stata 13 (StataCorp. 2013; StataCorp LP, College Station, TX).

Results

We restricted our analyses to a working-age population (<65 years old) reducing the derivation data set to 186 subjects and the validation data set to 190 subjects, a total of 376 subjects.

In the derivation data set, the median age was 46 years (interquartile range 18 years); 93 (50%) were male.

The performance of our best diagnostic algorithm (FVC < 70% predicted and FEV_1/FVC ≥ 70%) and four previously reported alternatives is shown in Table 1. It achieves a Sp of 96% and a PPV of 67 and 15% for a disease prevalence of 10 and 1%, respectively; false positives (n = 6) were fewer than those derived from other algorithms (n ranging from 56 to 74). In addition its high Sn (71%) produced the highest proportion of correctly classified restrictive cases (91%), corresponding to an overall accuracy, expressed as the area under the ROC curve of 0.87 (Figure 1).

We repeated these analyses using an alternative prediction equation (Crapo) to compare our results with the current standard one [2]. This increased the Sp of our algorithm: Sp (98%) and PPV (80 and 27% for a disease prevalence of 10 and 1%, respectively), with fewer false positives (n = 3) compared with previous algorithms (n ranging from 28 to 54). Again, the high Sn (71%) produced the highest proportion of correctly classified restrictive cases (93%), compared with previous algorithms (range 70–84%).

Finally, we tested the performance of the new algorithm in the validation data set of 190 subjects under the age of 65. The results were very similar; again it achieved the highest Sp (89–92% using Hankinson and Crapo predictive equations, respectively), corresponding to 15 and 11 false positives.

Discussion

We derived and validated a new spirometry-based diagnostic algorithm designed to be efficiently applied in respiratory surveillance in an occupational health setting. Our best diagnostic algorithm (FVC < 70% predicted and FEV_1/FVC ≥ 70%) produced a far lower number of false positives (n = 6; 4%) than previously published algorithms; in addition, its high Sn (71%) ensured a high percentage of correctly classified lung restrictive cases (91%). Our algorithm showed the best performance in a simulated population of working age and with a low prevalence of restricted lung impairment. However, we still recommend the use of the current standard diagnostic algorithm [2] in settings where very high Sn may be favoured.

Strengths of our analyses include our ability to validate the findings both 'internally', by applying two alternative predictive equations, and 'externally', by testing our algorithm in a comparable independent validation data set. In addition, the definition of true restrictive cases, used as a reference standard in our analyses, was based on state-of-the-art lung volume measurements. In fact, body plethysmography is generally considered the 'gold standard' for TLC measurement, except in subjects with very severe lung obstruction [9]. Limitations include that, apart from age and sex, we could not evaluate other potential confounding factors, such as smoking

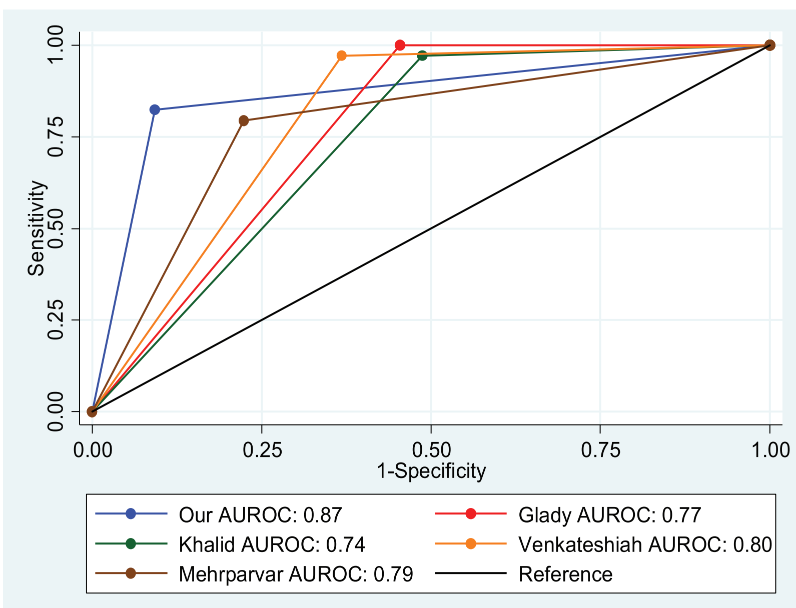

Figure 1. Receiver operating curves comparing the overall accuracy, expressed as area under the ROC curve (AUROC), of selected previous diagnostic algorithms versus ours using Hankinson prediction equations among adults aged under 65 years (n = 186).

or occupational exposures. In addition, all the subjects included in the analyses were ethnically 'White', so we cannot accurately predict results for other groups although we doubt they would differ importantly.

Our spirometry-based algorithm may be routinely adopted for respiratory surveillance in the workplace to reduce the proportion of false positives and thus unnecessary and expensive referrals for lung volume measurements.

Key points

- We derived and validated a new spirometry-based diagnostic algorithm designed to be efficiently applied in respiratory surveillance in an occupational health setting.
- Our best diagnostic algorithm (forced vital capacity < 70% predicted and forced expiratory volume in 1 s/forced vital capacity ≥ 70%) produced a far lower number of false positives (4%) than previously published algorithms; in addition, its high Sn (71%) ensured a high percentage of correctly classified lung restrictive cases (91%).
- Our spirometry-based algorithm may be routinely adopted for respiratory surveillance in the workplace to reduce the proportion of false positives and thus unnecessary and expensive referrals for lung volume measurements.

Conflicts of interest

None declared.

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