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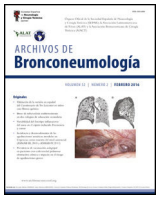

Scientific Letter

Accuracy of PIKO-6® and COPD-6® Devices in COPD Screening

To the Director,

COPD is a prevalent disease for which early diagnosis is essential.[1] The spirometrically determined ratio of the forced expiratory (FS) volume in 1 second (FEV_1) over the forced vital capacity (FVC) is the gold standard (GS) test to confirm the presence of airflow limitation. However, FS is frequently underutilized or unavailable in primary care (PC).[2–4] Because of easier performance and less variability, several studies have demonstrated that volume at six seconds (FEV_6) could be an acceptable alternative to FVC,[5,6] and so, the ratio of the FEV_1 over the volume measured at 6 s (FEV_1/FEV_6) could be a valid alternative to the ratio FEV_1/FVC obtained by FS.[7] Zhou et al.,[8] in a recent meta-analysis, concluded that micro-spirometers are "user-friendly, patient-friendly, inexpensive, and portable, making them suitable for PC use and providing a feasible pathway for early diagnosis of COPD"; moreover, their use could reduce underdiagnosis of COPD. The European Respiratory Society (ERS) has proposed investigating the role of these devices for early diagnosis.[9] The aim of our study was to validate COPD-6® and Piko-6®, the most widely studied micro-spirometers, for COPD screening and to determine the most accurate device for this task.

An observational prospective cross sectional study, calculated to require 569 patients (Epidat 4.2 program) to establish the potential differences between the selected micro-spirometers, recruited a total of 689 patients from the pulmonary outpatient departments at the University Hospitals of Salamanca and Zaragoza in Spain. The inclusion criteria were patients of both sexes, older than 35 years, smokers or ex-smokers with a history of more than 10 pack-years, regardless of whether they had respiratory symptoms. Patients who couldn't perform valid and repeatable spirometry or had absolute contraindications for the tests were excluded. The study was approved by the Ethics and Clinical Research Committee of the University Hospital of Salamanca.

All spirometry tests were performed by qualified operators according to the ERS/ATS spirometry standards, and were always carried out in the same order (FS, test with COPD-6®, test with Piko-6®). Variables recruited were: anthropometric data, symptoms, FEV_1, FVC and FEV_1/FVC obtained by FS, used as GS, and FEV_1, FEV_6 and FEV_1/FEV_6 obtained by COPD-6® and Piko-6® devices. Personnel conducting the tests ensured that patients rested between tests. Different statistical tests were used on the basis of the variable in question. A significance level of 0.05 was set in all analyses. The statistical tests used to compare the devices were Pearson correlations, Youden Index (YI), Kappa coefficient and ROC curves, and the analysis was performed with software by IBM SPSS 23 version.

Table 1
Percentage and Absolute Measurements of FEV_1, FVC and FEV_6 Obtained by Forced Spirometry (FS), and by the Devices Piko-6® and COPD-6® (Sample Size 664).

Sample Size 664	Data Expressed as Average and Standard Deviation		
	FS	Piko-6®	COPD-6®
FEV_1 (%)	81.15 (48.52)	71.06 (26.83)	79.9 (30.04)
FEV_6 or FVC (%)	100.08 (51.60)	81.15 (48.52)	82.5 (24.21)
FEV_1 (ml)	2303.30 (987.97)	2000.87 (886.98)	2158.71 (969.35)
FEV_6 or FVC (ml)	3577.03 (1042.26)	2936.43 (998.72)	2800.87 (1025.12)

ml = milliliters.

A total of 664 subjects from the total of 689 recruited (491 males, 173 females) met the criteria for inclusion. Average age 61.5 ± 11 years; 338 ex-smokers (51%) and 326 current smokers (49%); average pack-years 41.2 ± 22. Obstruction was defined as FEV_1/FVC < 70%. FS detected 411 COPD patients (62%), Piko-6® 340 (51%) and COPD-6® 209 (31.5%). Table 1 includes measurements for each variable. Compared to FS, percentages and absolute measurements for FEV_1 and FEV_6 obtained by hand-held expiratory flow meters were lower. Table 2 shows sensitivity, specificity, PPV, NPV and YI of both devices.

The Pearson correlation index of FEV_1 between FS and Piko-6® and between FS and COPD-6® was 0.94 and 0.97 respectively. Correlations of FEV_1/FEV_6 Piko-6® and COPD-6® were 0.79 and 0.73. Using FEV_1/FVC < 70% as a reference, the area under the ROC curve was 0.922 to Piko-6® and 0.913 to COPD-6®. YI of Piko-6® (greater relation between sensitivity and specificity) was higher at cutoff of <73% (YI = 0.74). When using COPD-6®, the sensitivity value was lower, so the cutoff point was 80%. The concordance observed between Piko-6® and FS was 83.9%, with a kappa value 0.67 ± 0.028. Moreover, COPD-6® concordance was 68.7% and the kappa value 0.42 ± 0.02.

COPD screening tools are needed to improve disease management. Our study was designed to evaluate the accuracy of Piko-6® and COPD-6® in the diagnosis of airway obstruction and to determine which is more reliable. Jing et al. meta-analyses[10] concluded that FEV_1/FEV_6 has a sensitivity of 89% (IC95%: 83–93%) and specificity of 98% (IC95%: 95–99%) in relation to FEV_1/FVC. Several authors[11–13] got good results with Piko-6®. In our study, FEV_1 and FEV_6 acquired by COPD-6® and Piko-6®, both in milliliters (ml) and percentage, were smaller than FEV_1 and FVC obtained by FS ($p = 0.001$).

There are two studies with similar objectives and design than ours: Represas et al.[14] with COPD-6® and Hidalgo et al.[15] with Piko-6®. Our COPD-6® results did not substantially differ from those of Represas. In both, FEV_1/FEV_6 was larger than FEV_1/FVC ($p < 0.001$), which was expected because of FEV_6 being lower than FVC. On this basis, the cutoff point for diagnosing obstruction should not be 0.7, since COPD-6® did not detect obstruction in almost half of

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Table 2
Patients Classified as COPD According to GOLD Criteria With the Three Devices: Forced Spirometry (FS), Piko-6® and COPD-6®. Sensitivity, Specificity, PPV, NPV and Youden Index (YI) With Piko-6® and COPD-6®, Reference Test Forced Spirometry (FS).

Patients Classified as COPD According to Gold Criteria With the Three Devices: Forced Spirometry (fs), Piko-6® and COPD-6®			
Diagnostic Test FS (Reference Test)	Airway Obstruction (COPD)	No Airway Obstruction (Healthy)	Total
	411	253	664
Diagnostic Test Piko-6®	Airway Obstruction (COPD)	No Airway Obstruction (Healthy)	Total
Positive	322	18	340
Negative	89	235	324
Total	411	253	664
	Value	CI (95%)	
Sensitivity (%)	78.35	74.24–82.45	
Specificity (%)	92.89	89.52–96.25	
Validity index (%)	83.89	81.01–86.76	
PPV (%)	94.71	92.18–97.23	
PNV (%)	72.53	67.52–77.55	
Prevalence (%)	61.9	58.13–65.67	
YI	0.71	0.66–0.76	
Diagnostic Test COPD-6®	Airway Obstruction (COPD)	No Airway Obstruction (Healthy)	Total
Positive	206	3	209
Negative	205	250	455
Total	411	253	664
	Value	CI (95%)	
Sensitivity (%)	50.12	45.17–55.08	
Specificity (%)	98.81	97.28–100	
Validity index (%)	68.67	65.07–72.28	
Predicted value + (%)	98.56	96.71–100	
Predicted value − (%)	54.95	50.26–59.63	
Prevalence (%)	61.9	58.13–65.67	
YI	0.49	0.44–0.54	

Abbreviations: YI, Youden Index; PPV, positive predictive value; NPV, negative predictive value; FS, forced spirometry; Validity index, diagnostic accuracy: (true positives + true negatives)/total × 100.

patients. In our study, we observed smaller differences of FEV_1 with respect to FS than Represas, with an average difference of 144 ml (IC 95%: 126–162) vs 167 ml (IC 95%: 144–190). In contrast, we found a greater difference in FEV_6. Similar to Represas, we found a good correlation between COPD-6® and FS, especially for FEV_1 measurement.

In Hidalgo's studio and ours FEV_1 and FEV_6 values with Piko-6® were also smaller than FEV_1 and FVC obtained by FS ($p < 0.001$), but there were not significant differences between FEV_1/FEV_6 and FEV_1/FVC. Hidalgo observed a good correlation with FEV_1, FEV_6 and FEV_1/FEV_6. Nevertheless, we noticed the best correlation with FEV_1 ($r = 0.94$ versus $r = 0.87$) and slightly worse with the ratio ($r = 0.79$ versus 0.94). Correlation could be considered excellent by linear regression lines.

We set out to determine the best FEV_1/FEV_6 cutoff point in terms of sensitivity and specificity to detect obstruction. However, FEV_1/FEV_6 acquired by micro-spirometers was greater than FEV_1/FVC, and so, a higher cutoff should be considered. To this aim, we used YI. The Piko-6® cutoff point of FEV_1/FEV_6 was 0.73 while with COPD-6® was 0.8 (considerably lower sensitivity). The cutoff point in the Represas,[15] Fritz,[11] Hidalgo,[14] and Van de Bemt[11] studies varied between 0.70 and 0.78. Represas concluded that when using COPD-6®, a cutoff point of 0.7 was not valid for COPD screening, and that a cutoff point of 0.75–0.80 was needed, in accordance with our results.

ROC curves were performed using $FEV_1/FVC < 70\%$ as a reference. For FEV_1/FEV_6 we noticed AUC 0.91 and 0.92 with COPD-6® and Piko-6®, respectively showing an excellent correlation with FS. Both devices showed an odds ratio higher than 20, the minimum needed to validate a test.

Chen et al.[16] stated that micro-spirometry was accurate and had clinical utility. In our research, Piko-6® showed a better concordance than COPD-6® classifying individuals as having COPD or healthy (COPD diagnosis excluded), although a possible limitation of our study is the fact that the tests were always performed in the same order and were not randomized. This study provides real-world evidence to identify best practices when screening for COPD using hand-held devices.

In conclusion, although FEV_1 and FEV_6 measurements undertaken with hand-held expiratory flow meters were lower than FEV_1 and FVC performed with FS, Piko-6® and COPD-6® are useful for COPD screening because correlation with FS is good. A FEV_1/FEV_6 cutoff point of 0.7 obtained by hand-held expiratory flow meters as COPD screening had false negative results, so, with portable devices, this cut-off point for detecting obstruction must be increased. The usefulness of hand-held expiratory flow meters for COPD screening could help reduce underdiagnoses of COPD and minimize workloads in lung function laboratories. We found Piko-6® to be the device of choice given that it achieves the best correlation with FS. Nevertheless, the exact role of micro-spirometers in the diagnosis process isn't yet fully established.

Contributing Authors

Miguel Ángel Hernández Mezquita and Alfonso Pérez Trullen: Study design, case inclusion, analysis of results and supervision of the final manuscript. Idania de Los Santos Ventura, Vanessa Hidalgo Sierra and Enrique Barrueco Otero: case inclusion and initial writing of the manuscript.

Statement of Ethics

This research was conducted ethically in accordance with the World Medical Association Declaration of Helsinki and approved by the ethics committee at Salamanca University Hospital on October 2, 2014. Approval code: PI 2014 10 01.

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Conflict of Interests

The authors have no conflicts of interest to declare.

Data Availability

No restrictions on data availability. Data statement: the data is available at: https://scholar.archive.org/work/ng6ecpnosrftzpkzvkyjhjrhtu.

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