A comparison of four tests of cognition as predictors of inability to perform spirometry in old age

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Abstract

Background: previous studies have shown that a Mini Mental State Examination (MMSE) score of <24/30 and inability to copy intersecting pentagons (IP) predicts inability to perform spirometry. We hypothesised that clock drawing tests (CLOX 1 and 2), being validated tests of cognitive executive function, might predict spirometry performance with a higher sensitivity and specificity than the MMSE or IP.

Methods: we studied 113 (84 females) spirometry-naïve inpatients, mean age of 84 years (range 74–97). All performed the MMSE, IP, CLOX 1 and 2 and then attempted to perform assisted spirometry to the American Thoracic Society/European Respiratory Society standard.

Results: of 113, 49 met the criteria for adequate spirometry. Using normative thresholds for probable impairment, inability to perform spirometry was predicted by MMSE <24/30 with a sensitivity of 81% and specificity of 90% (P < 0.0000); by inability to copy IP with a sensitivity of 92% and specificity of 100% (P < 0.0000); by CLOX1 <10/15 with a sensitivity of 81% and specificity of 49% (P < 0.001); and by CLOX2 <12/15 with a sensitivity of 63% and specificity of 65% (P < 0.0001).

Conclusion: CLOX tests did not perform better than MMSE and IP to identify subjects unlikely to be able to perform spirometry. Achieving assisted spirometry from the naïve state in old age might be more determined by global cognitive function and ideo-motor praxis than by executive control function.

Keywords: spirometry, elderly, cognitive function tests, MMSE, CLOX
Introduction

Spirometry is an important part of the diagnostic work up of patients with suspected asthma, chronic obstructive pulmonary disease (COPD) and other lung conditions and also provides useful objective information about responses to treatment and deterioration over time. The central role of spirometry in this context is embedded in national guideline recommendations [1] for the wider use of spirometry for the detection of COPD in hospital and community settings, with an emphasis on middle-aged and elderly people in whom the prevalence of COPD is high. Spirometry can be used alongside other clinical information to improve the diagnostic accuracy, assess disease severity and allow more rational treatment and management planning. Most of older patients can do adequate spirometry [2, 3]. However, it has been found that a proportion of elderly patients, particularly those more than the age of 75 years, and some younger patients, are unable to perform reliable full spirometry to measure FEV1 and FVC [2]. This ranged from ~12% of community dwelling older people [2] to 49% of elderly inpatients with indicators of frailty [3]. Further, it was shown that cognitive impairment was the most frequently encountered barrier to spirometry [2–6], and although the definitions of cognitive impairment varied between studies, the relationship with poor spirometry performance remained clear. It is important to identify patients who are unlikely to perform reliably, partly to avoid generating inaccurate indices that could lead to an incorrect diagnosis, partly to reduce the distress of repeated unsuccessful attempts and also to alert the clinician to the need to seek alternative information and evidence, particularly an enhanced history and physical examination, to reach a working diagnosis. In previous research, we showed that the Mini Mental State Examination (MMSE) and its intersecting pentagon-copying component (IP) predicted inadequate metered dose inhaler (MDI) performance with a high specificity but with moderate sensitivity [7], and in earlier work it was shown that acquisition of inhaler technique depends on global cognitive, ideo-motor and executive function [8–12]. The MMSE is a screening test of global cognitive function [13], while the act of doing spirometry properly would be expected to be dependent on adequate executive and ideo-motor (frontal and fronto-parietal) function, as is also the case for MDIs. Therefore, we hypothesised that screening tests that were designed to assess executive function might have a better overall predictive value than the MMSE for spirometry. The clock drawing tests CLOX1 and 2 [14] have an embedded executive and ideo-motor component and are validated for use in elderly subjects including those with indicators of frailty. CLOX1 involves asking the subject to draw a clock face on a blank sheet of paper and tests for executive dyscontrol in a novel and ambiguous situation, whereas CLOX2 requires the subject to copy a clock face and therefore tests ability to understand and plan a well-defined action then carry it out accurately and completely. Therefore, CLOX is used to detect abnormalities of executive control function such as goal selection, motor planning sequences, selective attention and self-monitoring of current action. To test our hypothesis, we conducted a study that compared MMSE, pentagon copying, CLOX1 and 2 as predictors of inability to perform standard spirometry.

Methods

We performed a prospective observational study of 113 patients (84 females) with a mean age of 84 years (range 74–97). All were in-patients receiving rehabilitation after an acute medical or surgical illness and had reached a stable clinical state at the time of recruitment. We studied subjects who were naïve to the procedure of spirometry in order to avoid the possibility that some patients with cognitive impairment might have retained a satisfactory technique from earlier in their clinical history. We recruited subjects who fulfilled the study criteria in chronological order of presentation, so the sample was quasi-random. The inclusion criteria were aged 70 years or more, willing to give written consent to perform spirometry and the cognitive tests. The exclusion criteria were severe dementia (a previous or current MMSE <11, partly because such patients were shown in our pilot studies to be unable to perform spirometry from the naïve state and partly on ethical advice that people with severe cognitive impairment would be unlikely to understand the study sufficiently to give informed consent), overt dyspraxia due, for example, to a stroke, impairment of vision or hearing to the extent that the patient could not understand the explanations and demonstrations of spirometry, contraindications to spirometry such as recent eye surgery or pneumothorax, asthma or COPD not yet stable after an exacerbation, delirium, severe communication difficulties due to dysphasia.

Spirometry was conducted on a single occasion by a fully trained researcher using a MicrolabsTM 3,000 portable spirometer including standard factory-set analytical software. The researcher used one-to-one explanation, demonstration and practice to prepare each subject for an attempt at spirometry. After preparation, individual patients made at least three attempts, and up to eight attempts were encouraged for those having difficulties achieving acceptable volume–time curves, if they were willing to keep trying to produce two acceptable and reproducible curves according to the American Thoracic Society/European Respiratory Society (ATS/ERS) criteria [15]. The time between attempts was 1–2 min and real-time visual displays of the spirometers were used during the procedure to help subjects to complete spirometry as accurately as possible. In accordance with the ATS/ERS criteria, accurate spirometry was considered achieved if the subject performed at least three acceptable attempts (no artefacts, satisfactory start, at least 6 s duration and/or 1 s final zero-flow plateau), two of which were reproducible (<200 ml difference between the curves at FEV1 and FVC). The data were recorded electronically and as printed graphs for subsequent analysis. The reasons for failing to meet the ATS/ERS criteria were recorded.
The MMSE, CLOX1 and CLOX2 were performed before spirometry by a separate observer trained to apply the tests in accordance with the published methods.

**Analysing the spirometry recordings**

A separate observer analysed the spirometry curves by taking into account the visual (printed graph) and electronic data in line with the ERS/ATS criteria, to ascertain whether the standards were met for full spirometry to FEV1 and FVC.

**Analysing the MMSE, pentagon copying, CLOX 1 and CLOX2**

The cognitive tests were scored according to the published criteria [13, 14]. A separate observer checked all the score sheets for consistency of scoring and adherence to the scoring criteria. In the small number of cases where a discrepancy was found, an agreed final score was made after discussion between the researchers. This also enabled the scoring of the intersecting pentagon (IP) component of the MMSE to be checked for strict concordance with the criteria before being extracted for separate comparison with spirometry performance. The IP was considered adequate (IP+) if it consisted of two shapes, each with five sides and five angles and two angles overlapping. Those not reaching that standard were scored IP−.

For the purpose of comparison between cognitive scores and spirometry performance, the thresholds taken as evidence of probable impairment [13, 14] were the normative levels described in the original validations and in use in clinical practice. For the MMSE and IP, these thresholds were in keeping with earlier studies in the same or similar circumstances [2–9]. Therefore, the cut-offs for comparison were set as MMSE <24/30, IP−, CLOX1 <10/15 and CLOX2 <12/15.

**Statistical method**

Categorical data were compared using Yates’ chi-squared test. Calculation of predictive values and categorical testing was performed using online software.

**Results**

The ATS/ERS spirometry standard was reached by 49/113 (43%) of the subjects. The most frequently observed reasons for not meeting the standard were failure to complete the forced expiratory manoeuvre, not taking a full deep breath in before starting forced expiration, not reaching or sustaining forced expiration, breathing alternately in and out through the apparatus, premature cessation due to coughing, progressively sub-maximal efforts and inability to start spirometry due to being unable to comprehend the procedure. Visual analysis of the spiromgrams showed that cognitively impaired subjects (MMSE <24) usually failed to meet the criteria for dyspraxic reasons whereas those with an MMSE >23 usually failed because of coughing or fatigue.

![Image](https://academic.oup.com/ageing/article-abstract/38/5/537/2462151/539)

Table 1. Comparison of MMSE, IP, CLOX1 and CLOX2 at normative thresholds in relation to ability of elderly subjects to perform spirometry to the ATS/ERS standard

<table>
<thead>
<tr>
<th>Cognitive test</th>
<th>Number of subjects able to perform spirometry</th>
<th>Number of subjects unable to perform spirometry</th>
<th>P-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>MMSE &lt; 24</td>
<td>5</td>
<td>52</td>
<td>0.0000</td>
</tr>
<tr>
<td>MMSE ≥ 24</td>
<td>44</td>
<td>12</td>
<td></td>
</tr>
<tr>
<td>IP−</td>
<td>0</td>
<td>59</td>
<td></td>
</tr>
<tr>
<td>IP+</td>
<td>49</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>CLOX1 &lt; 10</td>
<td>25</td>
<td>52</td>
<td>0.0000</td>
</tr>
<tr>
<td>CLOX1 ≥ 10</td>
<td>24</td>
<td>12</td>
<td>0.001</td>
</tr>
<tr>
<td>CLOX2 &lt; 12</td>
<td>17</td>
<td>40</td>
<td></td>
</tr>
<tr>
<td>CLOX2 ≥ 12</td>
<td>32</td>
<td>24</td>
<td>0.001</td>
</tr>
</tbody>
</table>


Table 2. The sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) of the four cognitive tests as predictors of inability to perform spirometry

<table>
<thead>
<tr>
<th>Cognitive test</th>
<th>Sensitivity % (95% CL)</th>
<th>Specificity % (95% CL)</th>
<th>PPV % (95% CL)</th>
<th>NPV % (95% CL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>MMSE &lt; 24</td>
<td>81 (69–90)</td>
<td>70 (59–81)</td>
<td>91 (80–97)</td>
<td>99 (91–100)</td>
</tr>
<tr>
<td>IP−</td>
<td>92 (82–97)</td>
<td>100 (94–100)</td>
<td>100 (92–100)</td>
<td>91 (79–97)</td>
</tr>
<tr>
<td>CLOX1 &lt; 10</td>
<td>80 (69–90)</td>
<td>49 (35–63)</td>
<td>68 (56–78)</td>
<td>67 (49–81)</td>
</tr>
<tr>
<td>CLOX2 &lt; 12</td>
<td>63 (49–74)</td>
<td>65 (50–78)</td>
<td>70 (56–81)</td>
<td>57 (43–70)</td>
</tr>
</tbody>
</table>

95% CL = 95% confidence limits. N = 113.

Table 1 shows a comparison of MMSE, IP, CLOX1 and CLOX2 scores at normative thresholds with ability to perform spirometry. Table 2 summarises the overall predictive value of the cognitive tests as predictors of inability to meet the ATS/ERS spirometry standard. It can be seen that the MMSE and IP as a separate test had better overall predictive power than the CLOX tests. Furthermore, for CLOX1, the sensitivity and specificity could not be improved by setting any other threshold except a score of 14/15, which was reached by only four subjects. For CLOX2, no better performing threshold could be applied. There appeared to be no components of CLOX1 or CLOX2 that were of any predictive utility, unlike IP (a component of MMSE) that performed well.

It was also found that no subject with an MMSE <18 and only two subjects with an MMSE <20 were able to meet the criteria. This finding is in keeping with previous research [5, 6].

**Discussion**

The results of this study did not confirm the outcome predicted by our hypothesis. Despite being configured and validated as tests of executive control function, CLOX1 and CLOX2 performed considerably less well than MMSE, which is a global cognitive screening test, and IP, an MMSE component that tests ideo-motor praxis. These findings are unlikely to be due to fundamental design problems with CLOX
because validation studies showed a high level of internal and inter-rater consistency and a broad concordance with established cognitive and executive screening tests [14]. One possible explanation is that the act of performing supervised spirometry might be less determined by executive control function than we have assumed. CLOX1 tests for executive dyscontrol in a novel and ambiguous situation, so it does not really reproduce the cognitive demands of a spirometry session. The dynamic relationship between patient and technician that appears to be an important determinant of a successful first attempt at spirometry might be closely linked to global cognitive integrity, and therefore more accurately reflected in the MMSE score. On the other hand, if that were the case, then the strong predictive performance of IP, which can be regarded as a test of ideo-motor praxis that is similar to CLOX2 (clock face copying), would not be expected. Indeed, CLOX2 performed only marginally better than CLOX1 as a predictor of an inadequate spirometry technique. Also, the process of explanation, demonstration and practice that precedes an attempt at spirometry might be as dependent on short-term memory and attention as it is on executive function, which could also account for the relatively superior predictive value of MMSE compared to CLOX. It is also possible that the case mix of patients differed sufficiently from that in the CLOX validation studies to reduce the apparent concordance between MMSE and CLOX in our study. The validation was carried out in healthy free-living elderly people and nursing home residents with probable Alzheimer’s disease, whereas our study included relatively physically frail patients with varying degrees of cognitive impairment due to a range of probable or proven causes including Alzheimer’s disease, Lewy body dementia, cerebrovascular disease and multi-infarct brain disease. Overall, our findings suggest that successful achievement of an assisted spirometry technique in spirometry-naïve elderly patients is more determined by global cognitive function and ideo-motor praxis than by mainly executive control function.

In terms of clinical utility, we have confirmed the findings of previous studies [5, 6] that indicate the potential role of the MMSE and its IP component in this context. The original MMSE and validated local versions are in widespread use in practice, so for a large proportion of frail elderly in-patients the information required to assess the likelihood of successful spirometry is readily available without the introduction of an unfamiliar cognitive test.

There are some alternative methods for assessing the airways function of subjects unable to perform spirometry, though most are not widely available. Partial spirometry to measure FEV1/FEV3 has been shown to be a feasible option for patients with mild cognitive impairment (MMSE 20–23) [3], though caution is required when interpreting the index. It has also been found that measuring airways resistance using the forced oscillation method can be used reliably in some patients with more severe cognitive impairment [4], though the technique is usually only available in specialised centres. The use of whole body plethysmography to measure airways resistance requires considerable patient co-operation and is not thought to be a suitable alternative, though there have been no studies of its use in subjects with cognitive impairment. For the future, research is currently being conducted to test a novel measure of the relationship between inspiratory effort and airflow that could lead to a practical alternative for patients unable to perform spirometry [16].

Key points
- Patients with a MMSE score of <24/30, or inability to copy overlapping pentagons, are rarely able to perform adequate spirometry.
- The MMSE and copy overlapping pentagons are more useful than CLOX for predicting inability to perform spirometry on old age.
- Performing a reliable spirometry manoeuvre appears to be more dependent on intact global cognitive function and ideo-motor praxis than on executive control function.

Conflicts of interest
None declared.

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Ethical approval
Dorset LREC.

References
A comparison of four tests of cognition


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