

Home-Based System for Recording Pulmonary Function and Disease-Related Symptoms in Patients with Chronic Obstructive Pulmonary Disease, COPD-A Pilot Study

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Keywords COPD assessment test; Exacerbation; Inspiratory capacity; Spirometry; Telemonitoring; Telemedicine

Abbreviations COPD: Chronic Obstructive Pulmonary Disease; CAT: COPD Assessment Test; IC: Inspiratory Capacity; MRC dyspnoea scale: Medical Research Council dyspnoea scale; TLC: Total Lung Capacity; HRQoL: Health-Related Quality of Life; FEV: Forced Expiratory Volume; FVC: Forced Vital Capacity

Abstract

Introduction: Many patients with Chronic Obstructive Pulmonary Disease (COPD) suffer from acute exacerbations characterized by an increase in symptoms beyond normal day-to-day variation. The prognosis of patients with frequent exacerbations is poor and effort to curb these worsening episodes has great potential to improve the patient's quality of life and to reduce associated costs. Telemonitoring has been proposed as a promising strategy in this respect. However, information on what physical signs or symptoms that should be recorded and how recorded data should be interpreted is largely missing in the literature.

Methods: A new home-based system, based on a tablet computer, which can guide COPD patients to perform spirometry (inspiratory capacity, IC and forced expiratory volume in one and six seconds, FEV₁ and FEV₆) and record symptoms (COPD assessment test, CAT) was developed. The system was evaluated for 8-12 weeks in four patients with moderate to severe COPD with the aims to; i) assess the feasibility of the system to be used unsupervised by COPD patients and, ii) to evaluate the quality and ability of recorded parameters to reveal early signs of an exacerbation. Pearson bivariate correlation was performed between all outcome measures and descriptive information about inherent subject properties were presented.

Results: The system was well accepted by all study subjects and the study generated a total of 253 measurements of which 94.5% were considered acceptable for analysis. One of the subjects developed an acute exacerbation towards the end of the study, whereas the other three subjects remained stable. Descriptive analysis of the data suggest that trends in the CAT score may indicate changes in health status and that IC tends to be more responsive to these changes compared to FEV₁.

Conclusion: The system developed in this study is well suited to be used unsupervised by COPD patients. Recorded data, in particular CAT, may be sensitive enough to detect early signs of an acute COPD exacerbation, although more data is needed to fully resolve the nature of such an association.

Introduction

Chronic Obstructive Pulmonary Disease (COPD) is a disease of growing global concern. It is characterized by a chronic obstructive airflow limitation, secondary to airway inflammation, and emphysematous changes in the lung. COPD is further associated with several systemic manifestations linked to impaired functional capacity, such as heart failure, osteoporosis, malnutrition, muscle wasting, depression, reduced balance and increased risk for falls [1-4]. Consequently, COPD patients typically suffer from a considerable restriction in physical activity level and poor quality of life. In addition to being ill-fated for the patient, low physical activity level and Health-Related Quality Of Life (HRQoL) have shown to be strong predictors of poor health outcome and are therefore important to assess as part of any disease management protocol [5-9].

In all stages of COPD, but particularly in severe disease, many patients suffer from acute exacerbations. An acute exacerbation is defined as an acute event characterized by a worsening of a patient's respiratory symptoms that is beyond normal day-to-day variations, and leads to a change in regular medication [10]. Exacerbations have been shown to be involved in emphysema progression [11] and the prognosis of patients with frequent exacerbations is much worse than for patients with the same degree of COPD but without history of exacerbations [12]. Recurring exacerbations will also seriously compromise the patient's ability to return to the previous level of physical activity,

which can be detrimental to the patient, as physical activity level is the strongest predictor of all-cause mortality in COPD [9].

A clinical experience is that COPD patients who develop exacerbations often seek health care too late, either owing to lack of knowledge of the early signs of an acute exacerbation or as they neglect to admit the signs. This is the case despite that acute exacerbations can be compared to heart attacks in terms of morbidity and mortality [13-16]. There is an urgent need for novel strategies and pro-active care models to address and reduce the health consequences, as well as the social and economical burden of COPD exacerbations.

Telemedicine, used interchangeably with telemonitoring or telehealth, has been judged a reasonable strategy for reducing the burden of chronic diseases by offering the opportunity to provide extended clinical support in the patients' home. Telemonitoring has been shown to be generally clinically effective in COPD, particularly with respect to preventing exacerbations and hospital admissions [17-19]. However, some studies are challenging these results [20,21] and there are significant inconsistencies in recent studies [1,22]. Most of these studies had a common aim; to evaluate the effect of telemonitoring on exacerbation rates and healthcare utilization, although the technological setup and design varied. How gathered data is analyzed and interpreted is rarely reported and empirical evidence on what parameters that actually reflect the current health status of COPD patients is to large parts missing.

The aims of this pilot study were to: i) assess the feasibility of a newly developed home-based system for recording pulmonary function and disease-related symptoms, and ii) evaluate the COPD patients' compliance when using the system both unsupervised and for an extended period of time. The system includes protocols for recording the lung function parameters Inspiratory Capacity (IC), Forced Expiratory Volume in One (FEV₁) and in six seconds (FEV₆), and symptoms through the validated COPD Assessment Test (CAT) [23].

Materials and Methods

System design

To be able to record lung function (IC, FEV₁ and FEV₆) and CAT in a home environment, a new home-based system for recording pulmonary function and disease-related symptoms was developed and implemented on a Windows 7 tablet computer (Acer Iconia Tab W501P, 2011). Software was developed to guide the users to record high-quality spirometry data without professional guidance, and to allow regular symptom reporting, according to the validated CAT questionnaire. The system utilizes a spirometer (SpiroTube Mobile Edition, Thor Laboratories, Hungary), which has a simple design allowing measurement of several lung function values, including IC. The application was designed to minimize the computer interaction required to initiate and complete the protocols and displayed two active buttons for activating the lung function test (spirometry) and the symptom-reporting tool (CAT) respectively. The only additional feature was a calendar, which displayed a record of completed measurements and indicated on what days the measurements should be performed. Permission to use CAT on a mobile platform was obtained from Glaxo Smith Kline (GSK) in 2010. The GSK clearly stated that the content and formatting of the CAT test should be kept and that all questions have to be visible to the subject at the same

time. Hence, only minimum adjustments to the layout were made to make the CAT test fit the screen of the tablet computer.

Subjects and study design

To evaluate the ability of the chosen parameters (IC, FEV₁, FEV₆ and CAT) to reveal early signs of exacerbations, a pilot study was performed in the homes of four subjects. Ethical approval was received from the Regional ethical review board at Umea University in 2011 (2011-09-31M). Subjects with moderate to severe COPD were recruited from the Department of Medicine, Division of Respiratory Medicine and Allergy, University Hospital, Umea, Sweden. After obtaining informed consent, subjects completed an outpatient visit that included standard medical examination, chest x-ray, dynamic spirometry, venous blood tests and two standardized six-minute walk tests [24]. The subjects were also asked to complete the MRC dyspnoea scale, which provided a baseline value of the subject's perceived respiratory disability [25]. Spirometry, MRC scale, venous blood sampling and six-minute walk test were also repeated at the end of the study.

Before returning home after the initial examinations, the subjects received a brief (15-20 minutes) introduction to the developed system. The subjects were instructed by experienced personnel in spirometry performance and tested the system according to the protocol that they had consented to follow at home for 8-12 weeks. This protocol should be followed by the subjects every day, twice a day (morning and evening) during the first week of the study and twice a day, three days a week (Tuesday, Thursday and Saturday) for the remaining weeks. The CAT score was shown to the subjects, whereas IC and FEV₁ and FEV₆ values were blinded to the subjects.

After completion of the study, the subjects were asked to answer a questionnaire regarding their experiences using this system. This questionnaire aimed at providing information on system performance, user acceptance, whether the study subjects perceived the spirometer maneuvers to be strenuous to perform, whether the subjects wished to see the spirometer values, as well as whether this procedure was considered to interfere with their daily life and activities or not. The questionnaire was designed with 12 statements, such as "To perform the measurements disturbed my daily activities", which were answered by a six-point ordinal Likert rating scale. The scale was scored 0=strongly disagree to 5=strongly agree.

Statistics

All statistics were analyzed using PASW Statistics (release 18.0.3, SPSS Inc., Chicago, IL, USA). Pearson bivariate correlation was performed between all outcome measures (i.e., IC, FEV₁, and CAT score) after removal of each subject's outcome baseline levels. $P < 0.05$ was applied as the level of two-tailed significance for each pairwise correlation measure. Outliers were identified according to Tukey's hinges using the third and first quartile.

Results

Data quality and compliance

Despite being performed unsupervised and in an uncontrolled environment, the home spirometry protocol produced acceptable spirometry results for all four subjects. The complete study generated a total number of 253 measurements of which 94.5 % were considered

Table 1: Information about data quality and user compliance.

	Total	Subject 1	Subject 2	Subject 3	Subject 4
Number of measurements	253	43	52	84	74
Missed occasion [%] ^a	16 [6.3 %]	3 [7.0 %]	0 [0 %]	8 [9.5 %]	5 [6.8 %]
Additional measurements [%] ^b	6 [2.4 %]	0 [0 %]	1 [1.9 %]	4 [4.8 %]	1 [1.4 %]
Unusable data [%] ^c	14 [5.5 %]	4 [9.3 %]	2 [3.8 %]	5 [6.0 %]	3 [4.1 %]
Redone measurement [%] ^d	37 [14.6 %]	1 [2.3 %]	1 [1.9 %]	20 [23.8 %]	15 [20.3 %]

^aEither spirometry, CAT or both were not completed.

^bAny measurement performed outside of the fixed protocol.

^cThe number of days that contained unusable data.

^dRedone measurement refers to occasions where the subject followed the protocol but a maneuver was not performed to satisfaction and had to be redone.

acceptable for analysis. However, since no quality indicators were implemented at this point, we applied less strict criteria for the spirometry measurements compared to the standards defined in the study by Miller, et al. [26], which required at least three acceptable recordings. Hence, we included IC, FEV₁ and FEV₆ in our assessment when a minimum of one acceptable measurement was recorded. Regarding compliance to the protocol, the test subjects failed to perform only 16 of the 253 scheduled measurements and 6 additional non-scheduled measurements were performed to make up for the data loss according to our instructions. Thirty-seven measurements were repeated, of which the majority were forced expiratory maneuvers performed by the two subjects who suffered from more severe COPD. Information about data quality and user compliance is presented in (Table 1).

User acceptance

The home-based system was well accepted by all users. All four subjects reported that the system did not disturb their daily activities and they all agreed that the integrated instructions were sufficient for performing the maneuvers. There was in addition a high agreement that the brief introduction at the start of the study was sufficient to learn how to operate the equipment, although two subjects reported that the instruction was slightly insufficient for understanding the tablet computer, and one subject indicated that the instructions for the spirometer could be improved. Two of the four subjects stated that there had been a few problems with the tablet computer and one subject reported that there had been some complications with the spirometer. On the statements addressing whether the system made the subjects more aware of their symptoms and whether the subjects wanted to see their spirometry values or not, there were fewer

consensuses. One subject strongly agreed that the technology made them more aware of their symptoms, whereas one strongly disagreed with this statement. The other two subjects weakly disagreed with the statement that the technology made them more aware of their symptoms. With respect to feedback on the spirometer values, two subjects strongly agreed that feedback on the spirometry is wanted and the additional two were slightly in favor. One subject found both IC and FEV to be very strenuous to perform, whereas one did not find any of the maneuvers demanding. The remaining two subjects agreed that the forced expiratory maneuver was slightly more strenuous to perform than the inspiratory maneuver. Finally, the COPD assessment test was considered to describe their symptoms fairly well, although only one subject strongly agreed with this statement.

Clinical outcomes

The complete system was piloted in the home of four subjects (subject 1-4) with moderate to severe COPD based on post-bronchodilator FEV₁ (FEV₁ of 53, 72, 44 and 39 % of predicted, respectively). For a summary of the study subjects, see (Table 2). The four subjects used the system for 8-12 weeks, starting with an intense week, during which measurements were performed twice a day (morning and evening) to make the subjects familiar with the equipment, and to establish a baseline. Of the four subjects enrolled in the study, three subjects (subject 1, 2 and 4) remained stable, whereas subject 3 experienced an acute exacerbation leading to hospital admission 9 days after the end of the study (Figure 1). The acute exacerbation resulted in a further increase in airflow limitation and post-bronchodilator FEV₁ was reduced from 44 % to 34 % of predicted. The MRC score did not change between baseline and after

Table 2: Anthropometric information and summarized clinical outcomes.

	Subject 1	Subject 2	Subject 3	Subject 4
Patient summary	Male 69 years 76,2 kg 176 cm	Female 77 years 84,7 kg 160 cm	Female 75 years 92,0 kg 164 cm	Female 73 years 45,0 kg 159 cm
Post-bronchodilator FEV ₁ [% predicted]	53 %	72 %	44 %	39 %
At baseline	51 %	66 %	34 %	35 %
After the study				
MRC Score				
At baseline	1	4	3	4
After the study	1	4	4	3
Six-minute walk test [m]				
At baseline (average)	518	262	292	291
After the study	532	300	255	304
Outcome (exacerbation)	no exacerbation	no exacerbation	exacerbation	no exacerbation

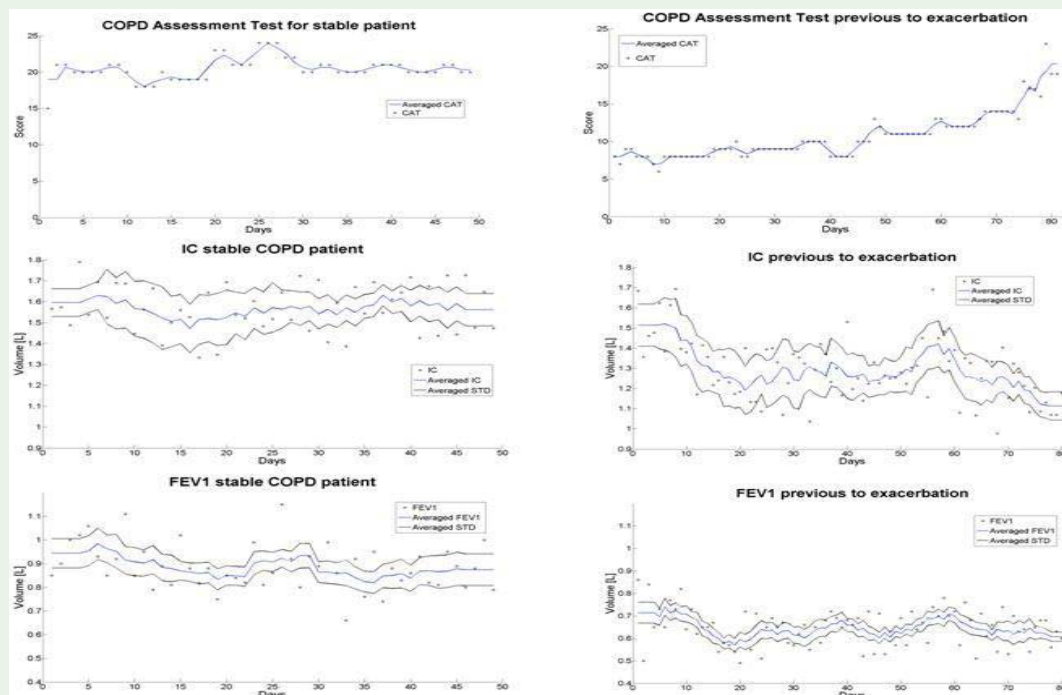


Figure 1: Illustration of records from a stable and an exacerbating subject. The patient was hospitalized due to exacerbation 9 days after the end of the study

the study. However, the outcome of the six minutes walk test increased for all subjects except for subject 3. The subject characteristics and clinical outcomes are summarized in (Table 2).

Upon inspection of all four spirometry time series, we clearly distinguish what can be called a learning effect, meaning that the IC and FEV_1 values varied for all subjects during the first couple of days to become more stable about a week into the study. A closer inspection of the spirometry data of subject 3, who experienced an exacerbation, further revealed a decline in IC, whereas FEV_1 remained stable. This indicates that IC may be more sensitive to deterioration in lung function compared with FEV_1 , when disregarding the learning effects. However, above all, in subject 3, we identify a very clear increase in CAT, which seems to be most sensitive to changes in health status

Table 3: Correlation between clinical outcomes.

		With exacerbating subject			Without exacerbating subject		
		IC	FEV_1	CAT	IC	FEV_1	CAT
IC	Pearson Correlation	1	,174*	-,334**	1	-,119	-,090
	Sig. (2-tailed)	n.a.	,011	,000	n.a.	,166	,296
	N	217	216	217	137	136	137
FEV_1	Pearson Correlation	,174*	1	-,127	-,119	1	,080
	Sig. (2-tailed)	,011	n.a.	,063	,166	n.a.	,354
	N	216	216	216	136	136	136
CAT	Pearson Correlation	-,334**	-,127	1	-,090	,080	1
	Sig. (2-tailed)	,000	,063	n.a.	,296	,354	n.a.
	N	217	216	217	137	136	137

*. Correlation is significant at the 0.05 level (2-tailed).

**. Correlation is significant at the 0.01 level (2-tailed).

Table 4: Descriptive information about clinical outcomes.

Subject		IC [L]	FEV_1 [L]	CAT[a.u]
1	N	34	34	34
	Mean	1,77	,56	5,2
	Std	,02	,04	1,4
2	N	45	45	45
	Mean	1,61	,29	20,0
	Std	,04	,018	3,5
3	N	80	80	80
	Mean	1,30	,33	10,4
	Std	,08	,01	3,1
4	N	58	58	58
	Mean	1,14	,31	14,4
	Std	,07	,01	1,1

compared to all other parameters evaluated throughout the course of this pilot study. In addition, the bivariate correlations between the different clinical outcome measures are shown in (Table 3). As can be seen, there is a weak but significant correlation between IC and FEV_1 and between IC and CAT. Summarized information about patient outcomes are presented in (Table 4).

Discussion

In this pilot study, we have developed and tested a new tool with the potential to record two particularly promising early markers of COPD exacerbations; the lung function value IC, which in relation to the Total Lung Capacity (TLC), has been shown to correlate with increased risk of severe exacerbations and mortality in COPD [27,28]

and CAT, which was recently suggested to provide a reliable score of exacerbation severity [29]. Whilst the number of subjects in this pilot study was small, the study produced high quality time series of data from three stable and one exacerbating subject. The CAT score appears to be sensitive to changes in health status, both in stable subjects and in the subject that experienced an acute exacerbation. This is in accordance with a recent study evaluating the correlation of daily CAT scores with health status, although this study focused on improvement in health status after acute exacerbations [30]. Moreover, descriptive analysis of the data suggest that trends in the CAT score may indicate changes in health status and that IC tends to be more responsive to these changes compared to FEV_1 . However, more data is needed to verify this correlation. IC is a marker of hyperinflation, i.e. trapped gas in the lungs due to expiratory flow limitations. An acute increase in hyperinflation has been associated with exacerbations and IC has been shown to correlate better with functional capacity than airflow limitation (FEV_1) during such events [31]. However, exacerbations are also associated with worsening of airflow obstruction and we expected to observe changes also in FEV_1 , though this was not evident here. Exacerbation-induced changes in IC and FEV_1 may have different time windows. A change in post-bronchodilator FEV_1 was indeed evident at follow-up (Table 2).

Telemonitoring is a concept that is currently attracting a lot of attention owing to ageing populations, shortage of health care personnel and a rapid increase in the prevalence of chronic diseases. Blood pressure, lung function, oxygen saturation, weight, physical activity and blood glucose are some parameters that are frequently measured at home as part of different telemedicine programs [19,32-34]. Still, there is inconclusive evidence of the benefits of these programs, both with respect to cost effectiveness [35,36] and clinical outcomes [20]. In some cases, this can be explained by differences or weaknesses in study design. It can also be a result of limited knowledge on what physiological and subjective parameters that is of actual clinical value, how they vary with time for a certain individual, how other risk factors affect the patterns of symptoms and what magnitude of changes that should trigger a response from the health care provider. In the case of COPD, there is a prominent lack of such knowledge.

Our study is too small in scope to declare a specific timeframe for the development of symptoms before an acute exacerbation. The symptoms and the severity of an exacerbation tend to vary between individuals due to inherent differences in the subjects' characteristics and the presence of various co-morbidities. Larger-scale studies on both stable and exacerbating subjects are thus needed before we can identify thresholds and potential patterns of events leading to an exacerbation. We can conclude that the system evaluated in this study is a good tool for generating such information, in contrast to many commercially available instruments. There are already a plethora of different telemedicine systems available on the market, including pulmonary diagnostics instruments. However, many consider spirometry, which is the golden standard for diagnosing and monitoring the progression of COPD, a practical art, which requires guidance by a trained health professional to produce reliable results. Our concept has shown to be well suited for unsupervised spirometry and we obtained high data quality despite measurements being performed in uncontrolled environments. To our knowledge, no other tele-spirometry system offers these features. Moreover,

IC is not a common feature in any of the telemedicine spirometry devices available on the market, which makes this system one of few feasible ways of evaluating the potential of IC to reveal early signs of exacerbations. The present study also had several limitations; we had not implemented any quality algorithms in the software at the time of the pilot, which leaves room for significant improvement in data output. Such algorithms can provide feedback on the quality of the measurements to the user and ensure that we obtain three acceptable measurements at each session. The gold standard for spirometry includes measurement of Forced Vital Capacity (FVC) in addition to FEV_1 and the ratio is thus FEV_1/FVC [10]. In this study we chose FEV_6 in order to standardize the measurement at home. However, as we were primarily interested in the FEV_1 , this deviation should not affect the results of the study. Moreover, we did not require our subjects to wear a nose clip, which is recommended and even required for an IC protocol to comply with the standards. Hence, we expect the next generation of the system to produce even better outcomes.

Finally, to be able to generate a sustainable disease management concept for individuals suffering from COPD based on telemonitoring, we need to address more than technical challenges as discussed in this paper; there is also a need to develop new disease management strategies with the capacity to interpret and respond properly to the gathered information in a way that can increase the patients' awareness of symptoms, change their health seeking behavior and improve their self efficacy to better cope with the disease. Not until then, telemonitoring will be of value for the patient and result in a desirable reduction in exacerbations and health care utilization for patients with COPD.

Conclusion

In this pilot study, we have provided evidence that measuring pulmonary function, using a newly developed system, is feasible and that recorded data, particularly CAT but also IC, appear highly responsive to changes in health status among patients with COPD. Hence, this concept could be a powerful complement to strategies aiming to detect and treat early symptoms of acute exacerbations to prevent unnecessary hospital admissions and improve the prognosis for the patient with COPD. However, more data is needed to fully explore what changes in the recorded parameters that should trigger a response, either from the system itself or from the health care provider receiving the data.

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