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Concise report

Feasibility of online home spirometry in systemic sclerosis–associated interstitial lung disease: a pilot study

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Abstract

Objectives. Frequent monitoring of forced vital capacity at home may be of added value in patients with SSc-associated interstitial lung disease (SSc-ILD) to monitor disease progression and guide treatment decisions. The aim of this study was to evaluate the feasibility and optimal frequency of online home spirometry using a home monitoring application in patients with SSc-ILD.

Methods. This was a prospective, observational study in patients with SSc-ILD. Patients evaluated for 3 months the online home monitoring application ILD-online integrated with a Bluetooth-connected spirometer. Patients performed daily home spirometry for 6 weeks and weekly home spirometry for 6 weeks. In addition, patients completed an evaluation questionnaire after 3 months and online patient-reported outcomes at baseline and 3 months.

Results. Ten consecutive patients participated. Mean adherence to home spirometry was 98.8% (S.D. 1.5). Home and hospital spirometry were highly correlated. The mean coefficient of variation was lower for weekly [2.45% (S.D. 1.19)] than daily [3.86% (S.D. 1.45)] forced vital capacity measurements ($P = 0.005$). All patients considered the home monitoring application and spirometer easy to use and no patients considered home spirometry burdensome. All patients would recommend home monitoring to other patients with SSc.

Conclusions. Home spirometry using an online home monitoring application is feasible in patients with SSc-ILD, with high adherence and patient satisfaction. Larger long-term studies are needed to assess whether home spirometry can detect the progression of ILD in patients with SSc.

Key words: SSc, interstitial lung disease, home spirometry, eHealth, home monitoring

Rheumatology key messages

- Online home spirometry is feasible and reliable in patients with SSc-ILD, despite potential disease-specific hurdles.
- Patient satisfaction with the online home monitoring application and adherence to home spirometry were high.
- Within-patient variability of weekly FVC measurements was lower than variability of daily FVC measurements.

Introduction

SSc is an autoimmune disorder characterized by microvascular damage, immune dysregulation and fibrosis in multiple organs [1]. Pulmonary involvement is common; early autopsy studies showed that interstitial fibrosis was present in 74–100% of SSc patients [2, 3]. More recently, interstitial abnormalities on high-resolution CT scan have been reported in up to 90% of patients and between 40–75% of patients have restrictive changes in pulmonary function tests (PFTs) [4]. Analyses by the EULAR Scleroderma Trials and Research Group revealed that interstitial lung disease (ILD) is frequently present in dcSSc (53%) and lcSSc (35%) and is the leading cause of death in these patients [5, 6]. SSc-

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CLINICAL SCIENCE

associated ILD (SSc-ILD) has a variable clinical course. Especially in early ILD, discriminating between potentially stable and progressive disease is challenging.Treatment of SSc-ILD consists of immunosuppressive therapy, such as MMF or CYC, with some efficacy [7]. Recently nintedanib, an antifibrotic drug, has also been shown to slow down forced vital capacity (FVC) decline in patients with SSc-ILD [8]. As immunosuppressive therapy may have the most profound effect early in the course of SSc-ILD and most common practice is to start therapy as soon as lung function declines, regular assessment of PFTs is crucial and is the cornerstone of longitudinal follow-up of SSc patients [9]. FVC decline is considered to be a reliable criterion for SSc-ILD progression, particularly in patients with an established diagnosis of ILD and patients with lung function that is already abnormal. Monitoring of FVC is believed to be inappropriate for 'very mild' ILD and for ILD screening purposes [10].

Serial PFTs are mainly used to monitor disease progression and the necessity to intensify treatment. Moreover, short-term trends in lung function can also predict mortality [11]. As the decline in FVC in SSc-ILD is slower than in a disease like idiopathic pulmonary fibrosis (IPF), measurement variability and actual deterioration may be difficult to distinguish [8]. By collecting frequent data points, a more accurate representation of the disease course can be obtained, which can help to guide treatment decisions and facilitate monitoring of disease progression.

Recently an online home monitoring application, including home spirometry and patient-reported outcome measures (PROMs), was developed together with IPF patients [12, 13]. Daily home spirometry yielded reliable results in this patient group and patient satisfaction with the application was high. Similar results have been shown in a pilot study in sarcoidosis patients [14]. Although home monitoring may have several potential advantages in SSc-ILD, it has never been evaluated in this patient group to date. There may be disease-specific hurdles that can complicate the use of a home monitoring application in SSc, including microstomia and finger deformities causing reduced hand function.

The aim of the current study was to evaluate the feasibility of an online home monitoring application, including home spirometry, in patients with SSc-ILD. Furthermore, we aimed to assess whether the results of home spirometry are comparable to hospital-based PFTs and evaluate the optimal frequency of home spirometry.

Methods

This was a prospective, observational study performed in the Department of Rheumatic Diseases of Radboud University Medical Centre in Nijmegen, a tertiary referral centre for SSc in the Netherlands. Inclusion criteria were a diagnosis of SSc with associated ILD and age >18 years. Included patients fulfilled the ACR/EULAR classification criteria for SSc [15]. Associated ILD was established by the treating physician based on a high-resolution CT scan and PFT results. Patients were excluded if they were unable to speak, write and read Dutch or had no internet access at home. This study complies with the Declaration of Helsinki and was approved by the local ethics committee. All patients gave written informed consent.

Patients were asked to use the CE-marked home monitoring application ILD-online for 3 months (Curavista, Geertruidenberg, The Netherlands). This is a secured online application integrated with home spirometry using a Bluetooth enabled handheld spirometer (MIR, Spirobank Smart, Italy), online PROMs, an overview of results over time, an eConsultation option and an information library. At baseline, patients received a 20 min training about the use of the application and the spirometer. An additional mouthpiece and stylus pen were provided if needed, to increase user convenience. Patients were considered sufficiently trained if they were able to perform three reproducible FVC measurements with <150 mL difference in the two highest FVCs. Patients were asked to undertake one spirometry measurement each day for 6 weeks and three spirometry measurements once a week for the other 6 weeks. Half of the patients started with weekly home spirometry and the other 50% of patients started with daily home spirometry. Patients were instructed to perform spirometry at approximately the same time every day to reduce variability [16]. Measurements were sent directly to the hospital via an encrypted connection. To evaluate health-related quality of life (HRQOL), anxiety and depressive symptoms, patients completed the following PROMs at the start of the study and after 3 months: the King's Brief Interstitial Lung Disease (K-BILD) questionnaire, the Hospital Anxiety and Depression Scale (HADS) and the EuroQoL 5-Dimensions 5-Level questionnaire (EQ-5D-5L) [17–19]. The K-BILD is a 15-item questionnaire concerning three domains: breathlessness and activities, psychological and chest symptoms. It has been validated in ILD and the minimal clinically important difference is 3.9 points; scores range from 0 to 100, with higher scores corresponding with a better HRQOL [17]. The EQ-5D-5L comprises five questions and a visual analogue scale on general health status, with scores between 0 and 100 [18]. The HADS contains seven questions about anxiety and seven questions about depressive symptoms, with scores ranging from 0 to 21. A score of ≥ 8 indicates anxiety or depression [19]. After 3 months, patients completed a 15-item evaluation questionnaire regarding their experiences with the home monitoring program. At baseline and after 3 months, in-hospital PFTs were performed.

Statistical analysis

Within-patient variability of FVC was evaluated using the coefficient of variation (CoV), using 'detrended data points' to allow for potential changes in FVC over time. The CoV was measured separately for the daily and

weekly spirometry periods; CoVs of both periods were compared with paired *t*-tests. The Spearman correlation coefficient was used to correlate home with hospital spirometry, using the mean value of home-based FVC during 3 months and the mean value of hospital FVC at baseline and 3 months. Adherence to home spirometry was calculated by dividing the actual number of home spirometry measurements by the expected number of home spirometry measurements during the study period and presented as a percentage. Within-patient differences in PROMs were analysed with paired *t*-tests. Analyses were performed in R version 3.6.2 (R Foundation for Statistical Computing, Vienna, Austria) and SPSS Statistics version 25.0 (IBM, Armonk, NY, USA). Data are presented as mean (S.D.) or median [interquartile range (IQR)].

Results

Ten consecutive patients participated; mean age 60.3 years (S.D. 9.9), 60% female and 70% had dcSSc (Table 1). Nine patients completed the study and one patient discontinued early due to an autologous stem cell transplantation for progressive SSc.

Feasibility and reliability of home spirometry

Mean adherence to home spirometry was 98.8% (S.D. 1.5). The mean values of home and hospital FVC were highly correlated ($r = 0.99$, $P < 0.001$). Overall the median value for home-based FVC was 230 mL (IQR 0.16–0.37) or 6.0% (IQR 4.5–9.0) lower compared with hospital-based FVC. The mean variability (CoV) for daily FVC measurements was 3.86% (S.D. 1.45) and the mean CoV for weekly FVC measurements was 2.45% (S.D. 1.19). The CoV of daily FVC measurements was significantly higher than the CoV of weekly FVC measurements [difference 1.39% (95% CI 0.54, 2.23), $P = 0.005$]. An example of home and hospital FVC measurements of one patient during the study is provided in Fig. 1.

Table 1 Baseline characteristics of study patients ($N = 10$)

Baseline characteristics	Values
Female, *n* (%)	6 (60)
Age, years, mean (S.D.)	60.3 (9.9)
lcSSc, *n* (%)	3 (30)
dcSSc, *n* (%)	7 (70)
Years since first non-RP symptom, median (range)	8 (1–12)
Modified Rodnan skin score, mean (S.D.)	7.8 (7.4)
Facial involvement, *n* (%)	7 (70)
Maximum mouth opening, mm, mean (S.D.)	45 (6)
ANA positive, *n* (%)	10 (100)
Anti-Scl-70	5
Anti-centromere	1
Anti-RNA polymerase III	1
Anti-fibrillarin	1
FVC, % of predicted value, mean (S.D.)	78.5 (16.2)
DLCO, % of predicted value, mean (S.D.)	55.8 (21.4)
Receiving immunosuppression, *n* (%)	9 (90)
Mycophenolate mofetil, *n* (%)	9 (90)
Average dose, mg/day	2444
K-BILD total score, mean (S.D.)	65.74 (10.32)
EQ-5D-5L index value, mean (S.D.)	0.82 (0.12)
EQ-5D VAS score, mean (S.D.)	72.26 (26.77)
HADS anxiety score, mean (S.D.)	4.11 (2.09)
HADS depression score, mean (S.D.)	3.11 (2.57)

DLCO: diffusion capacity of the lung for carbon monoxide; VAS: visual analogue scale.

Patient-reported outcomes

In general, patient experiences with home monitoring were positive. All patients considered the home monitoring application and spirometer easy to use and were able to place their mouth around the spirometer mouthpiece without any difficulties. No patients considered home spirometry burdensome. Almost all patients (90%) found it pleasant to see an overview of their lung function over time and would be willing to perform weekly FVC measurements for a prolonged period of time for study purposes. The majority of patients (70%) stated that home monitoring could provide them with more insights into their disease course. Only two patients reported that they had encountered minor technical issues, mainly concerning the connectivity between the spirometer and the application. Finally, all patients would recommend home monitoring to other patients with SSc and 90% would like to continue the use of the home monitoring application in routine daily care.

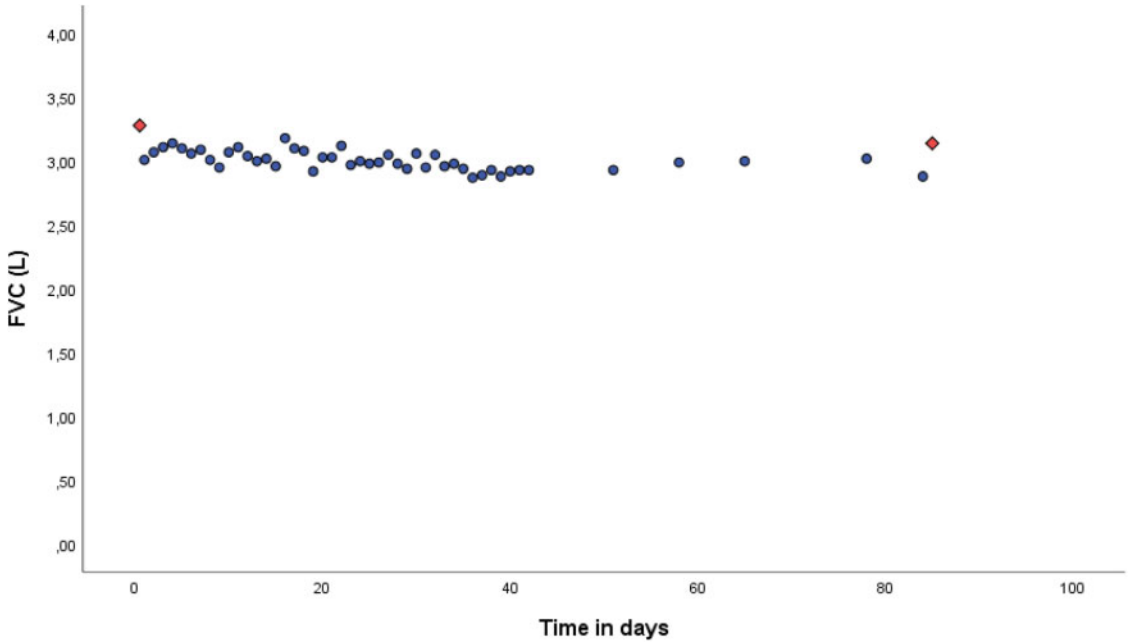
The QOL measured by the EQ-5D-5L index value [difference −0.06 (95% CI −0.15, 0.03), $P = 0.16$] and the EQ-5D visual analogue scale score [difference −1.26 (95% CI −6.53, 4.01), $P = 0.60$] did not change over time. The K-BILD total score decreased, with a mean of 4.02 points (95% CI −7.4, −0.67; $P = 0.024$). One patient reported anxiety and one patient reported depressive symptoms at both time points. Overall, scores for anxiety [difference 0.57 (95% CI −0.54, 1.65), $P = 0.28$] and depressive symptoms [difference 0.11 (95% CI −0.60, 0.82), $P = 0.73$] remained stable over time.

Discussion

To our knowledge, this is the first study assessing the feasibility of an online home monitoring application, including home spirometry, in patients with SSc-ILD. Patient satisfaction with the application and adherence to home spirometry were high and patients considered home spirometry not burdensome at all. Correlation with hospital-based spirometry was high. Overall, results of home-based FVC were lower than hospital-based FVC, which is in line with previous home spirometry studies in other ILDs [12, 14, 20].

The mean within-patient variability in FVC measurements was low. Interestingly, variability was significantly lower during the weekly spirometry period than the daily spirometry period. The most likely reason for this is that patients performed three consecutive measurements a

Fig. 1 Example of home and hospital FVC measurements of one patient during the study



The first 6 week period consisted of daily spirometry measurements and the second 6 week period consisted of weekly spirometry measurements.

day during the weekly period (of which the best FVC was automatically selected) and only one FVC measurement a day during the daily period. Multiple daily measurements are generally considered too intrusive if patients perform spirometry every day [13, 21]. Our findings imply that weekly measurement of three consecutive FVCs can potentially decrease variability and may be a good alternative to a single FVC measurement each day, although this is partly dependent on the specific research question.

In the field of ILD, home spirometry has gained increasing attention in the last few years. The first studies in IPF revealed that home spirometry yielded reliable results, predicted disease progression better than hospital spirometry and could potentially decrease sample sizes for future clinical trials [20, 22]. However, in the study by Johannson *et al.* [20], adherence to home spirometry decreased over time. Lung function data collected by patients in these studies were written in a paper-based diary or stored in a central database, without an option to share the measurements directly with healthcare providers. A recent randomized trial with pirfenidone in unclassifiable ILD used home spirometry (FVC) as the primary end point [21]. Unfortunately, the primary outcome could not be analysed as planned, due to the high variability of home-based FVC measurements. This high variability was probably caused by a lack of good instruction regarding home spirometry, adherence problems and technical problems with the hand-held spirometers [21]. The online home monitoring program used in the current study yielded similar results in IPF, sarcoidosis and other forms of pulmonary fibrosis, with a low variability in home-based FVC and a small number of technical issues and missing data [12–14, 16]. Hence we believe that most issues raised in previous studies can be addressed by the use of an online system with direct data transmission to the hospital, low-threshold communication, e-mail reminders and feedback on the quality of the measurements. Importantly, home monitoring was highly feasible in SSc patients, despite presumed disease-specific hurdles. None of the patients had difficulties with performing spirometry, as an additional mouthpiece was provided that was easier to use for patients with a limited mouth opening. Even patients with finger deformities were able to perform online PROMs on a smartphone or tablet with a stylus pen. This underlines the importance of identifying and addressing the needs of specific patient populations when using eHealth applications [12].

Anxiety and depression scores were within the normal range in all but one patient and did not change during the study, demonstrating that home spirometry does not lead to increased anxiety and depression levels. The mean K-BILD total score significantly declined during the study, corresponding with a deteriorating HRQOL. However, because of the limited sample size, the decrease in the K-BILD score should be interpreted with caution. In the original validation study of the K-BILD questionnaire, a limited number of patients with CTD-ILD were included, but larger validation studies in SSc-ILD are lacking [17].

Limitations of this study include the small sample size and single-centre design. Nevertheless, we believe that the findings in this pilot study are encouraging and open up new possibilities for future studies with home monitoring in SSc-ILD.

In conclusion, home spirometry using an online home monitoring application is feasible in patients with SSc-ILD, with high patient satisfaction and adherence. Larger long-term studies are needed to assess whether home spirometry can detect the progression of ILD in patients with SSc.

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Data availability statement

Data are available upon reasonable request by any qualified researchers who engage in rigorous, independent scientific research, and will be provided following review and approval of a research proposal and Statistical Analysis Plan (SAP) and execution of a Data Sharing Agreement (DSA). All data relevant to the study are included in the article.

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