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Original article

Quality of life and functional disability in patients with interstitial lung disease related to Systemic Sclerosis

Federica Lumetti[1], Lissette Barone[1], Cristina Alfieri[1], Mario Silva[2], Valter Serra[3], Giovanni Delsante[1], Nicola Sverzellati[2], Alarico Ariani[1]

[1] Medicine Department, Internal Medicine and Rheumatology Unit, University Hospital, Parma, Italy; [2] Department of Clinical Sciences, Section of Radiology, University of Parma, Italy; [3] Cardiopulmonary Department, Cardiology Unit di Cardiology, University Hospital, Parma, Italy

Summary. *Background:* Systemic Sclerosis (SSc) is a connective disease impairing respiratory function. SSc worsens patients' Health Assessment Questionnaire (HAQ-DI), Short Form 36 Physical and Mental Component Summary (SF36-PCS and SF36-MCS). The aim of this work is to verify whether there is correlation between quality of life and lung interstitiopathy in SSc patients. *Methods:* SF36 and HAQ-DI were given to each patient (48 in all). Lung involvement was evaluated with Baseline Dyspnea Index (BDI), spirometry and pulmonary fibrosis radiological assessment (PFRA). Correlations between SF36, HAQ-DI and lung involvement severity were investigated with Spearman's rank test. A p-value<0.05 was considered statistically significant. *Results:* SF36-PCS and SF36-MCS correlate with BDI (respectively rho=0.553 p=0.0001; rho=0.357 p=0.0150). The best correlating SF36 subsets are Physical Role (rho =0.566 p<0.0001) and Bodily Pain (rho=0.444 p=0.0020). BDI correlates with HAQ-DI (rho=-0.655 p<0.0001). No statistically significant correlation was found between SF36, HAQ-DI and spirometrical values nor PFRA. *Conclusions:* The SSc patients enrolled have an impaired quality of life as widely demonstrated in literature. Quality of life reduction and functional ability decrease are only related to respiratory subjective impairment (assessed by BDI). Actually no correlation with objective lung damage (assessed by spirometry and PFRA) was detected. (www.actabiomedica.it)

Key words: scleroderma, health related quality of life, interstitial lung disease, dyspnea

Introduction

Systemic Sclerosis (SSc) is an autoimmune and microvascular disease related to a multi-systemic impairment such as skin thickening, digital ulcers, lung fibrosis, pulmonary arterial hypertension, renal failure and gastro-oesophageal reflux disease (1,2).

Although SSc is an extremely heterogeneous disease, there are two types of subsets on the basis of the cutaneous manifestations. Diffuse cutaneous systemic sclerosis (dSSc) is characterised by a skin involvement proximal to the elbows and knees in addition to the trunk. Limited cutaneous systemic sclerosis (lSSc) is identified by a skin involvement distal to elbows and knees (3).

SSc is strongly associated with an increased mortality and morbidity, depressive symptoms, disability, recurring health care use and productivity losses (4,5). As a consequence there is a worsening of the Health–related quality of life (HRQoL) (6). The HRQoL in SSc patients can be assessed by self-administered questionnaires. In particular the Medical Outcome Survey Short Form 36 (SF36) is suitable for an overall evaluation of perceived physical and psychological

health (7,8). The Health Assessment Questionnaire Disability Index (HAQ-DI) is the most common and widely used tool to investigate the functional disability perspective (9,10).

The most frequent pulmonary involvement in SSc is the interstitial lung disease (ILD) which represents the main disease-related cause of death (11-13). ILD requires a multimodal assessment through pulmonary function tests (PFTs), pulmonary fibrosis semiquantitative scores based on chest Computed Tomography (CT) and evaluation of clinical manifestations due to breathlessness (14).

The aim of this work is to verify whether there is a correlation between the HRQoL and ILD assessment in SSc patients. We have specifically focused our attention on the correlations between dyspnea, PFTs values, ILD semiquantitative radiological scores, SF36 and HAQ-DI.

Methods

The present study was conducted according to the Declaration of Helsinki and approved by the local Ethical Committee. All recruited subjects signed an informed consent form before participating in the study.

Subjects

Fourty-eight (48) consecutive patients admitted to the our Clinic between September and December 2013 were enrolled. Each one had a diagnosis of limited SSc established according to Le Roy and the ACR/EULAR classification criteria (3,15). Exclusion criteria were: age < 18 years, presence of pulmonary arterial hypertension (according to an echocardiography performed by an experienced cardiologist, SV), presence of obstructive pulmonary disease signs at HRCT or PFTs, informed consent absence, incomplete questionnaires' compilation.

Functional disability assessment

Global functional disability was assessed by HAQ, a very user-friendly tool which was originally conceived to quantify rheumatoid arthritis patients' disability. Its application has also been extended and validated in SSc subjects. It consists of 20 questions divided into 8 domains: dressing/grooming, arising, eating, walking, hygiene, reach, grip; common daily activities. The score for each response ranges from 0 (no disability) to 3 (maximal disability); the final HAQ-DI score is calculated by averaging the highest score of each domain (16). For this study we used the Italian validated version (17).

Quality of life assessment

SF-36 is a self-administered questionnaire made up of 36 questions, which are grouped into 8 domains: physical function, physical role, bodily pain, general health, vitality, social function, emotional role, and mental health. Every single domain is scored separately and has a range from 0 (the worst result) to 100 (the best result). The domains' scores can also be encapsulated into the physical component summary (PCS) and the mental component summary (MCS) scores. PCS and MCS scores range from a minimum of 0 (the worst HRQoL) to a maximum of 100 (the best HRQoL) (18,19). Patients with hand-disability or comprehension difficulties were helped by the nursing staff (BL and AC).

Subjective ILD assessment

The most important clinical manifestation related to ILD is the dyspnea. The Baseline Mahler's Dyspnea Index (BDI) is a self-administered scale that the patient can easly fill out. BDI gives a breathlessness severity evaluation and it is made up by three different subsets: functional impairment, magnitude of task, magnitude of effort. Each of them is assessed with a 0 to 4 scale so the sum can range from 0 (severe dyspnea) to 12 (no limitations due to breath).

Objective ILD assessment

Spirometry is the main exam to evaluate the static and dynamic pulmonary volumes. Specifically we recorded the Forced Vital Capacity (FVC) and Diffusing Capacity of CO (DLco). To reduce measurement

variability we always used the same technique and the same laboratory. American Thoracic Society/European Respiratory Society (ATS/ERS) standards were adopted.

The ILD extent and severity was assessed on the basis of pulmonary fibrosis detectable on chest HRCT. HRCT was performed using 128-slice MDCT (Somatom FLASH, Siemens, Forcheim, Germany) in all cases. CT images were reconstructed at section widths of 1 mm using a high spatial frequency algorithm. All patients were examined in the supine position from lung apices to lung bases at full-suspended inspiration using standard acquisition parameters: 100 effective mAs, 120kVp. All images were viewed at window settings optimised for assessment of lung parenchyma (window width, 1600–1600 HU; window level, -500 to -600 HU). The pulmonary fibrosis radiological assessment (PFRA) consists in a semiquantitative evaluation of ILD extent to the nearest 5% according to Goh et al. method (20). PFRA was performed by an experienced chest radiologist (SN) who had no knowledge of lung function data or other indicators of disease severity.

Data Analysis

Non-parametric tests were used for all parameters. The Spearman rank order test was used to verify the correlation between PFTs, PFRA, questionnaires subset and total scores. Spearman rho < 0.30 was considered fair, 0.31-0.50 moderate, 0.51-0.70 good, 0.71-1.00 excellent. A p-value <0.05 was considered statistically significant.

Statistical analysis was performed by using R software (www.r-project.org with psy and ca package).

Results

The descriptive statistics of these patients are summarised in Table 1. The mean PCS- SF36 score is 35.87 (Confidence Interval 95%: 32.86-38.88) while the mean MCS-SF36 score score is 40.65 (CI 95%: 37.11-44.20). The mean score of each SF36 domain with the relative CI is shown in Figure 1.

Mahler's BDI has a good correlation with SF36-PCS (rho = 0.553 , p = 0.0001) and HAQ- DI (rho = -0.655 , p < 0.0001) and a moderate correlation with

Table 1. Enrolled patients' descriptive statistics

Characteristic	Results
Age, mean ± SD years	63.3 ± 11.7
Gender, % female	97.92%
Race/ethnicity	
Caucasian	95.84%
African	2.08%
Other	2.08%
SSc duration, mean ± SD years	10.6 ± 7.9
Weight, kg	64.1 ± 16.9
Current smoker, %	6.25%
anti-topoisomerase positive patients, %	31.25%

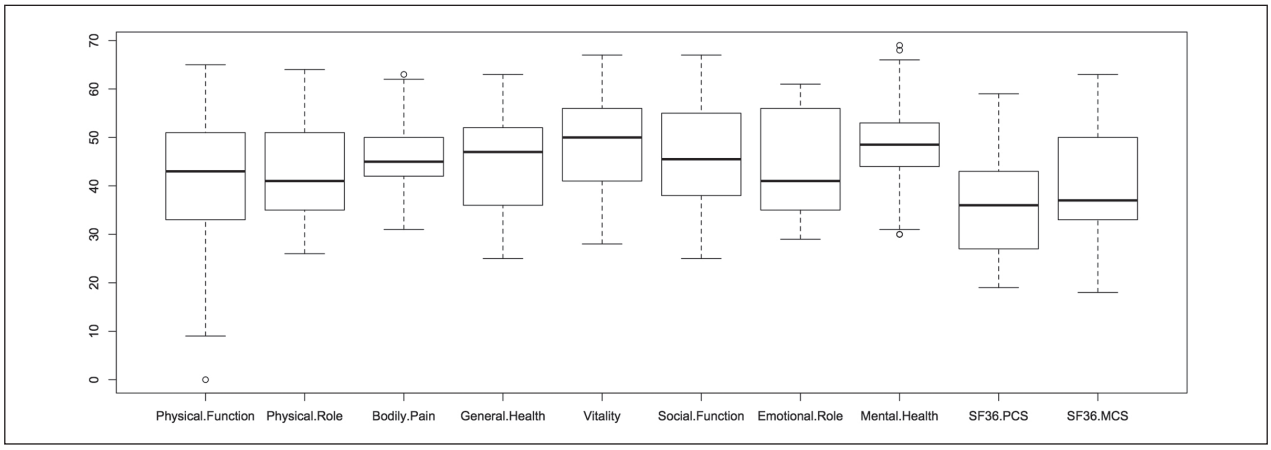

Figure 1.

Table 2. Correlation between Interstitial Lung Disease assessment, Short Form 36 and Health Assessment Questionnaire - Disability Index [SF36-PCS = Short Form 36 Physical Component Summary, SF36-MCS = Short Form 36 Mental Component Summary, HAQ -DI = Health Assessment Questionnaire - Disability Index, BDI = Baseline Dyspnea Index, FVC = Forced Vital Capacity, DLco = Diffusing Lung capacity of CO, PFRA = Pulmonary Fibrosis Radiological Assessment]

	SF36-PCS		SF36-MCS		HAQ-DI	
	rho	p-value	rho	p-value	rho	p-value
BDI	0.553	0.0001	0.357	0.0150	-0.655	<0.0001
FVC	0.018	ns	-0.153	ns	0.008	ns
DLco	-0.048	ns	-0.142	ns	0.177	ns
PFRA	0.182	ns	0.124	ns	-0.246	ns

Table 3. Short Form 36 (SF36) domains correlation with Baseline Dyspnea Index

SF36 Domain	rho	p-value
Physical Function	0.429	0.0029
Physical Role	0.566	0.0001
Bodily Pain	0.444	0.0020
General Health	0.358	0.0146
Vitality	0.443	0.0020
Social Function	0.302	0.0417
Emotional Role	0.266	ns
Mental Health	0.405	0.0053

SF36-MCS (rho = 0.357 ; p = 0.0150) (Table 2). Every SF36 domain (except for Emotional Role) had a moderate to good correlation with BDI as shown in Table 3; in particular the best SF36 subsets correlating with the dyspnea index are Physical Role (rho = 0.566 , p = 0.0001) and Bodily Pain (rho = 0.444 , p = 0.0020).

No statistically significant correlation was found between PFTs values, PFRA and SF-36 domains or component summary. As for SF36, the HAQ-DI does not correlate with PFTs or PFRA (Table 2).

Discussion

Patient reported outcomes have a remarkable importance in monitoring therapeutic results both in clinical practice and clinical trials. In recent years several studies dealing with HRQoL, disability and psychological involvement in SSc patients have been published (10,21-25). SSc is a chronic disease that may affect virtually every organ or tissue with the consequent functional disability and social restrictions (26-28). Thereby a mood disorder is more frequent in SSc patients than in other medical care recipients (29).

HAQ-DI is a self-reported and fast scoring questionnaire developed to patients' functional impairment evaluation. The clinimetric properties of this disability index were examined in depth so that it is extensively used in SSc studies. In fact HAQ-DI has shown a correlation with clinical SSc manifestations (30).

The HRQoL, assessed with SF36, is decreased both in diffuse and limited subset of SSc (7,31). Specifically the physical score was at least lower than 1 standard deviation in SSc patients compared with general population. Similarly the mental score in normal subjects was 0.5 standard deviation higher. Obviously the worst SSc skin subset was the diffuse one with SF36 scores 3.5 times lesser compared to the limited form (19).

Maybe the quality of life decrease is not only due to a long disease duration. In fact a physical and psychological worsening was observed even in patients with an early SSc diagnosis (32). So it appears reasonable that the poor HRQoL is also related to the disease activity or severity of symptoms. Interstitial lung impairment, which is the most frequent death cause in SSc, and its main clinical manifestation, dyspnea, have a deep repercussion on patients' existence. For example, in SSc patients with active alveolitis SF36 outcomes were globally reduced; however, whenever dyspnea was severe there was a consistent HRQoL impairment (33).

Dyspnea, although it is a really easy recognisable manifestation, can be quite barely measured. There are no dyspnea questionnaires completely validated in SSc but the Mahler's BDI was partially justified since being used in Scleroderma Lung Study (34,35).

Spirometry and chest CT can provide an assessment less dependent on patients' viewpoint. To date the loss of lung function is considered the best prognostic index in SSc-ILD. Pulmonary functional tests such as FVC and DLco have been used as primary endpoints in many studies because of their strong association with mortality (36).

Chest CT is the gold standard to detect pulmonary fibrosis; many authors managed to create a reliable semiquantitative assessment method to evaluate interstitial lung disease severity and extension. Goh and al. have introduced a simple and brief procedure based on chest CT examination (20). Moreover it was demonstrated that an extensive disease (i.e. more than 20% of lung involved by interstitiopathy) is related to an ominous prognosis (37).

In this study, we correlate HRQoL and disability function (respectively evaluated with SF36 and HAQ-DI) in SSC patients with the ILD severity assessed by Mahler's BDI, spirometry and semiquantitative radiological score based on pulmonary fibrosis detectable on chest CT.

Taking into account the above results the following observations can be drawn. First, PCS and MCS are essentially consistent with the scores founded by other Authors (31,38). In other words in this group of SSc enrolled patients it was ascertained a relevant physical and psychological deterioration. Second, the HAQ-DI worsening correlates with the Mahler's BDI reduction. This result underlines that the breathlessness has a negative weight on patients' perceived functioning limitation. The significant correlation between BDI and most of SF36 domains and component summaries can be considered as the consequence of the dyspnea detrimental impact on daily life. The psychological impairment seems to be widely due to a decrease in industriousness production efficacy and social dynamism (i.e. Vitality). Surprisingly, in our group, PFTs and PFRA negative values do not have any correlation with functional disability nor poor HRQoL. This observation can be explained through the fact that the lSSc patients become rarely aware of an actual lung function deterioration.

This study has some limitations. First of all, SSc enrolled patients are not very numerous. Moreover we did not perform any comparison between SSc subgroups (i.e. dSSc vs lSSc subjects). Finally we employed many self-administered questionnaires which can present some disadvantages in both questions' interpretation and in the actual compilation. In fact, SSc patients self-compilation of SF-36 can be more difficult because of the hands' muscle weakness or reduced fingers' range of movement (39). We have attempted to overcome this obstacle through the aid of qualified nursing staff who supported patients in reading and understanding the questions and, in some cases, helped directly in filling out the questionnaires. Therefore, patients showed a high degree of compliance in completing every form.

Summarising the dyspnea determines not only an impairment of daily life common activities but also affects the psychic sphere. Probably the anxiety generated by the symptom itself is experienced by the patient as an expression of a serious disease that implies a mood deflection. That is congruent with Arat et al assumption about the emotional responses to personal disease representation are major determinants of mental health (40).

Therefore in SSc assessment patients' impression must always keep in mind in spite of not being a match with any objective measurable data deriving from chest CT or PFTs. Indeed subjective perception of dyspnea can by itself negatively affect the HRQoL. Understanding how to mitigate the most disabling symptoms according to patient's opinion will be more and more crucial in one of challenges that a rheumatologist has to take on: the HRQoL improvement in SSc subjects.

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Correspondance:
Dott. Alarico Ariani
Azienda Ospedaliero Universitaria di Parma
Ospedale Maggiore di Parma
Day Hospital del Dipartimento Medico
Polispecialistico 2 - Reumatologia
Via Gramsci 14, 43100 Parma (Italy)
Tel. +390521/702776 +390521/702786
Fax +390521/704815
E-mail dott.alaricoariani@libero.it