

Improved Cough and Cough-Specific Quality of Life in Patients Treated for Scleroderma-Related Interstitial Lung Disease

Results of Scleroderma Lung Study II

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e-Appendix 1.

Justification for defining frequent cough (FC) based on the participant responses to the first two questions in the St. George's Respiratory Questionnaire (SGRQ):

Analyzing data from 4513 subjects with COPD in the COPDGene cohort, Kim et al.¹ have compared different definitions of chronic bronchitis, including the classic definition (cough and sputum on most days for at least 3 months a year for at least 2 years) and a definition based on responses to the first two questions in the SGRQ (*1. Over the past 3 months, I have coughed a) most days a week b) several days a week c) a few days a month d) only with chest infections and e) not at all; 2. Over the past 3 months, I have brought up phlegm [sputum] a) most days a week b) several days a week c) a few days a month d) only with chest infections and e) not at all.*) They found striking similarities in the clinical, radiographic and physiologic characteristics between the two groups of patients with chronic bronchitis defined by these two definitions, a finding that is not surprising since the first two questions in the SGRQ correspond well to the classic definition, except for the fact that the time frame for the SGRQ is only the past 3 months. Since the SGRQ was administered to all SLS II participants, we relied on the first two questions concerning cough and sputum, respectively, to define "frequent cough" with or without frequent sputum. We avoided the term "chronic" in view of the time frame of the past 3 months, rather than the past 2 or more years used in the classic definition of "chronic bronchitis". We also avoided the term "bronchitis" since cough associated with ILD, unlike that associated with chronic obstructive pulmonary disease, is often dry (without sputum production) and, instead, characterized the cough as "dry" or "wet". Moreover, we believe that our distinction between "frequent" cough and non-frequent cough is justified in view of the large gap between "most" or "several" days a week (the first two response options to question 1 in the SGRQ) and only "a few days a month" or "only with chest infection" (the next two response options in the SGRQ), the last option being "not at all".

¹**Kim V**, Crapo J, Zhao H, Jones PW, et al. Comparison between an alternative and the classic definition of chronic bronchitis in COPDGene. *Ann Am Thorac Soc.* 2015 Mar;12(3):332-9.

e-Table 1. Pearson correlations between cough-specific QoL (LCQ) scores and other baseline characteristics for patients with frequent cough at baseline

		Pearson Correlation Coefficient			
Baseline Features	N	total_lcq	Phys_lcq	Psyc_lcq	Soci_lcq
Demographics					
Age, yr	87	-0.023	0.002	-0.059	-0.007
Height, cm	87	-0.003	0.005	0.023	-0.014
Weight, kg	87	-0.107	-0.150	-0.084	-0.084
Scleroderma features					
Raynauds, yrs	87	-0.032	0.020	-0.003	-0.107
Non-Raynauds, yrs	87	-0.271*	-0.221*	-0.298**	-0.238*
Skin score, mRSS	87	0.208	0.243*	0.204	0.179
Pulmonary function					
FVC, % pred	87	0.232*	0.150	0.236*	0.267*
DLCO, % pred	87	0.258*	0.211*	0.28**	0.212*
HRCT Scores					
QLF_LM	83	-0.173	-0.096	-0.201	-0.190
QILD_LM	83	-0.200	-0.177	-0.217*	-0.184
QLF_WL	83	-0.245*	-0.214	-0.258*	-0.229*
QILD_WL	83	-0.25*	-0.294**	-0.252*	-0.183
HRQOL					
PCS_SF36	87	0.258*	0.378***	0.199	0.171
MCS_SF36	87	0.210	0.205	0.188	0.195
HAQ-DI	87	-0.036	-0.075	0.006	-0.030
Other symptoms					
BDI	80	0.389***	0.449***	0.347**	0.315**
VAS breathing	87	-0.355***	-0.333**	-0.269*	-0.35***
GERD score	87	-0.239*	-0.277**	-0.237*	-0.185

For definitions of abbreviations please see footnote to Table 1.

* p<0.05; **P<0.01; ***p<0.001

e-Table 2. Number of patients with cough and GERD data at both baseline and 24 months who reported frequent cough and/or GERD symptoms at each time point

	GERD present at baseline, absent at 24 months	GERD absent at baseline, present at 24 months	GERD absence at baseline and 24 months	GERD present at baseline and 24 months
Frequent cough present at baseline, absent at 24 months	5	0	4	19
Frequent cough present at both baseline and 24 months	3	7	3	25

e-Table 3. Mean (\pm SD) Leicester Cough Questionnaire (LCQ) scores (total and domain) at baseline and 24 months for both treatment arms separately and combined

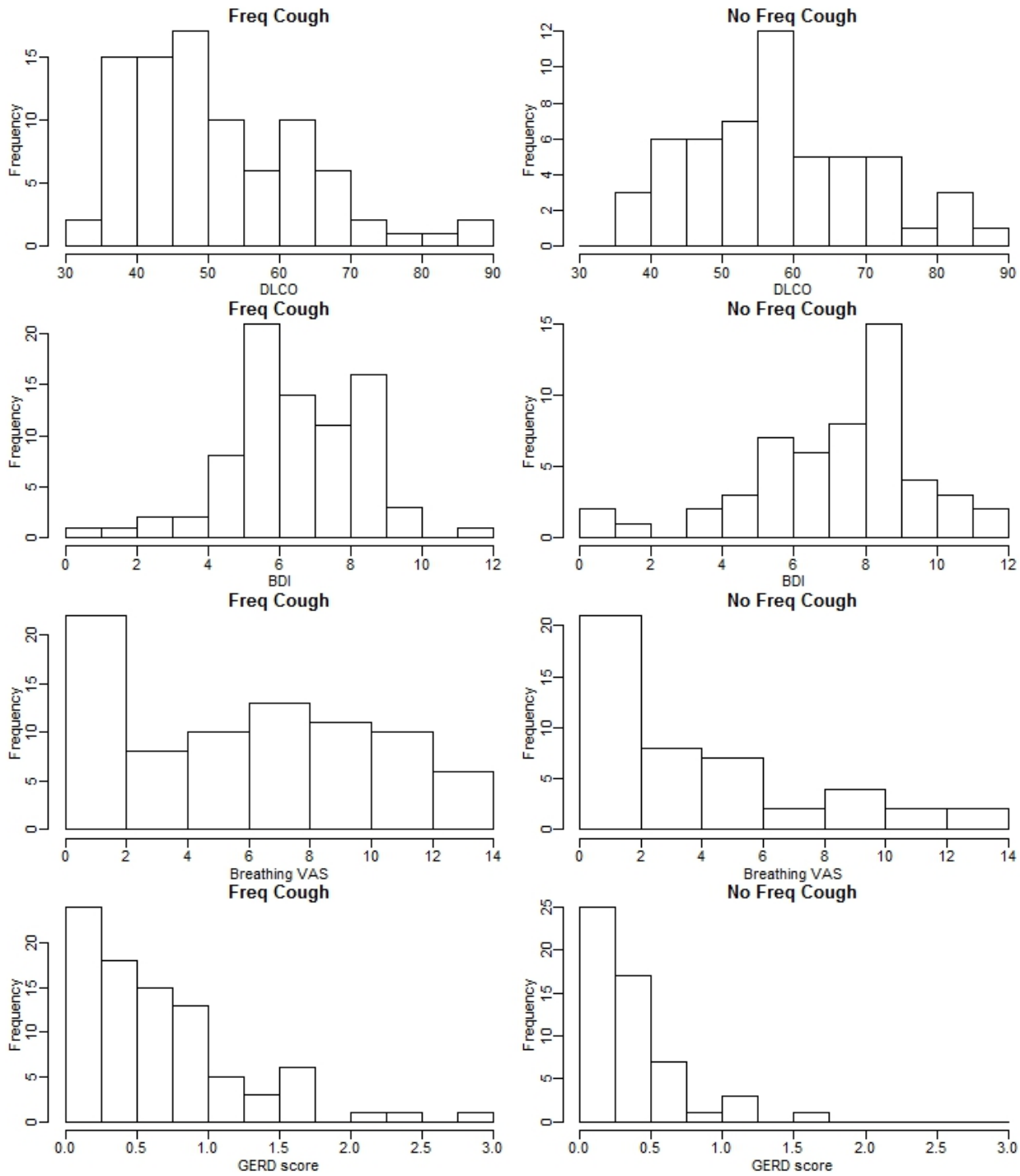
		Both Treatment Arms Combined	CYC (N=32)	MMF(N=34)
Total_LCQ scores (scale 3-21)*	Baseline	15.4 (3.7)	15.1 (3.6)	15.6 (3.8)
	24 months	16.7 (4.0)	16.2 (4.3)	17.1 (3.8)
Δ Total LCQ scores	Baseline - 24 months	0.8 (3.8)	0.8 (4.3)	0.9 (3.3)
Physical_LCQ scores (scale 1-7) [†]	Baseline	4.91 (1.1)	4.83 (1.1)	4.99 (1.0)
	24 months	5.32 (1.2)	5.19 (1.3)	5.45 (1.1)
Δ Physical LCQ scores [§]	Baseline-24 months	0.3 (1.2)	0.3 (1.3)	0.2 (1.1)
Psychological LCQ scores (scale 1-7) [†]	Baseline	5.20 (1.5)	5.10 (1.5)	5.26 (1.5)
	24 months	5.70 (1.5)	5.61 (1.5)	5.71 (1.6)
Δ Psychological LCQ scores	Baseline-24 months	0.3 (1.5)	0.3 (1.7)	0.2 (1.2)
		(1.5)		
Social_LCQ scores (scale 1-7) [†]	Baseline	5.31 (1.4)	5.19 (1.3)	5.44 (1.5)
	24 months	5.68 (1.5)	5.44 (1.7)	5.92 (1.3)
Δ Social LCQ scores	Baseline-24 months	0.2 (1.5)	0.1 (1.6)	0.3 (1.4)

*3=worst cough-specific QoL and 21=best; [†]1=worse QoL and 7=best

[†]1=worse QoL and 7=best

[§]None of the differences from baseline to 24 months are statistically significant

e-Figure 1A. Distribution of DLCO % predicted values and scores for BDI (total), breathing VAS and GERD (GIT-2) at baseline in patients stratified by the presence or absence of frequent cough.



e-Figure 1B. Distribution of scores for quantitative lung fibrosis in the whole lung (QLF-WL), quantitative total ILD in the whole lung (QILD-WL), QLF in the lobe of maximal involvement (QLF-LM) and QILD in the lobe of maximal involvement (QILD-LM) at baseline in patients stratified by the presence or absence of frequent cough.

