Published in final edited form as:

Br J Dermatol. 2017 January ; 176(1): 262–264. doi:10.1111/bjd.14771.

Pulmonary function tests, interstitial lung disease, and lung function decline in outpatients with classic and clinically amyopathic dermatomyositis

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Interstitial lung disease (ILD) is common among patients with both classic dermatomyositis (DM) and clinically amyopathic dermatomyositis (CADM), patients with classic skin manifestations without weakness.[1–3] ILD prognosis is thought to be worse in patients with CADM, but this observation may be due primarily to an increased frequency of rapidly-progressive ILD.[2,4–7] The objectives of this study were to compare the frequency of pulmonary function test (PFT) abnormalities and ILD in patients with DM and CADM and assess frequency of worsening PFTs.

Charts of 151 patients in a prospective cohort of outpatients with dermatomyositis presenting or referred to the Dermatology Department at the University of Pennsylvania were retrospectively reviewed through October 2014 to identify 128 patients with possible, probable, or definite adult DM based on Bohan and Peter Criteria or CADM as per Sontheimer[8], excluding juvenile DM or overlap syndromes.

PFTs were routinely ordered at the initial visit as part of standard practice and repeat testing was typically yearly or more frequently as clinically indicated. Abnormal PFTs were defined by FVC, TLC, or DLCO < 80% predicted. Significant decline in pulmonary function tests was a 15% decline in absolute values of DLCO or 10% decline in FVC or TLC at the last available PFTs.[9] To identify ILD, CT scans within 1 year of the first abnormal PFTs were blindly reviewed by an experienced radiologist (WM). T-tests, Wilcoxon rank-sum, and

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Conflicts of interest: None declared

Fisher's exact tests compared patients with DM and CADM with abnormal PFTs and compared patients with and without ILD.

PFTs were available in 69/76 (91%) patients with DM and 47/52 (90%) patients with CADM. Abnormal PFTs were present in 34/69 (49%) with DM and 20/47 (43%) with CADM ($p = 0.48$). Characteristics of patients with DM and CADM with abnormal PFTs were similar aside from creatine kinase levels (Table 1). DLCO, FVC, TLC, and PFT pattern at baseline were also similar. The most common pattern was an isolated reduction in DLCO.

Baseline CT was available for review in 39/54 (72%) with abnormal PFTs. ILD was present in 9/23 (39%) with DM vs. 6/16 (38%) with CADM ($p = 0.92$). Subjects with ILD had lower FVC, DLCO, and TLC than subjects without ILD (Table 2). All PFT patterns were represented in patients with ILD with 6/15 (40%) having restriction at baseline. 14/15 (93%) patients with ILD had an abnormal DLCO < 80% predicted. Lower DLCO cutoffs had higher specificity for ILD but with substantial loss in sensitivity. 5/15 (33%) of patients with ILD had neither cough nor dyspnea documented at baseline.

At last follow-up, PFTs declined in 4/15 (27%) patients with ILD - 2/6 (33%) with CADM and 2/7 (22%) with DM. Among patients with ILD, 3/4 (75%) with a decline in PFTs had a history of rapidly-progressive ILD compared to 1/11 (9%) without decline in PFTs.

Abnormal PFTs are common in patients with dermatomyositis and ILD is present in a subset, with similar rates in classic DM and CADM. ILD can occur with any PFT pattern, including an isolated reduction in DLCO, and in asymptomatic patients.

More than half of patients with abnormal PFTs had no CT evidence of ILD. Only a small proportion had other potential explanations for abnormal PFTs. Pulmonary hypertension and anemia were uncommon and muscle disease was typically well controlled. The subsequent development of ILD in one patient without ILD at baseline highlights the importance of repeat imaging if PFTs decline or symptoms progress.

Overall, one quarter of patients with ILD had a decline in PFTs, and there was 1 death among 15 patients with ILD during several years of follow-up. Most patients received aggressive immunosuppression. Notably, this relatively favorable prognosis applies to patients with chronic ILD followed in the outpatient setting. Patients with rapidly-progressive lung disease would not have been captured in this outpatient cohort during their initial pulmonary presentation. In addition, patients with UIP, severe ILD, or with certain autoantibodies that may have been underrepresented may have poorer prognosis.

Larger prospective studies that include patients with CADM are needed to inform prognosis of patients with chronic ILD. In previous studies, clinical deterioration was often dominated by the subset of patients with rapidly-progressive ILD, with most deaths occurring within the first year.[5,10] The number of patients with ILD in this study is too small to reliably examine prognostic factors but may be informative for future studies. PFTs declined at similar rates in CADM and DM, and it may be that autoantibodies are more important prognostically for ILD than the phenotype of muscle disease.

In summary, abnormal PFTs are common in patients with DM and CADM. ILD may be present with any abnormality in PFTs even in the absence of symptoms, but abnormal PFTs should not be assumed to represent ILD. Further studies to identify prognostic factors for patients with chronic ILD are needed.

Acknowledgments

Funding statement: Michael George is supported by the National Institutes of Health (NIH 5T32AR007442-28). Victoria P. Werth is supported by the Department of Veterans Affairs (Veterans Health Administration, Office of Research and Development, Biomedical Laboratory Research and Development) and by the National Institutes of Health (NIH R21 AR066286). Funders had no involvement in the study design, data collection, data analysis, manuscript preparation, and/or publication decisions.

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Table 1

Characteristics of patients with classic dermatomyositis versus clinically amyopathic dermatomyositis with abnormal pulmonary function tests

	Classic DM (n = 34)	CADM (n = 20)	p-value
Age, years	52.9 (11.4)	58.2 (13.2)	0.13
Female	25 (74%)	18 (90%)	0.18
Caucasian	29 (85%)	18 (90%)	1.0
Disease duration at baseline, years	1.5 [0.6, 7.2]	1.8 [0.9, 4.0]	0.94
Malignancy within 5 years of diagnosis	6 (18%)	2 (10%)	0.70
History of rapidly-progressive ILD[a]	2 (6%)	2 (10%)	0.62
Fever associated with DM	3 (9%)	3 (15%)	0.66
Raynaud's phenomenon	5 (15%)	4 (20%)	0.71
Inflammatory arthritis	7 (21%)	5 (25%)	0.74
Mechanic's hands	9 (26%)	10 (50%)	0.14
Ulcerating Gottron's	2 (6%)	0 (0%)	0.27
Echocardiogram with pulmonary hypertension (PASP ≥ 35 mmHg)	0/20 (0%)	3/12 (15%)	0.04
Creatine kinase at baseline, units/L	138 [70, 269]	52 [29, 97]	< 0.001*
Aldolase at baseline, units/L	4.4 [3.1, 5.9]	4.8 [4.4, 6.3]	0.30
Hemoglobin at baseline, g/dL	13.6 [12.2, 14.2]	13.5 [12.6, 14.1]	0.71
ANA ≥ 1:160	14/29 (41%)	6/18 (30%)	0.37
Anti-Jo-1 antibodies	4/21 (12%)	2/13 (10%)	1.0
Anti-SSA antibodies	3/22 (9%)	1/14 (5%)	1.0
Anti-RNP antibodies	1/10 (3%)	0/9 (0%)	1.0
Anti-MDA5/CADM140	0/0 (0%)	2/2 (10%)	–
DLCO % predicted	74 [64, 79]	67 [58, 72]	0.08
FVC % predicted	81 [71, 91]	88 [78, 97]	0.18
TLC % predicted	86 [77, 98]	87 [70, 98]	0.60
ILD present on CT scan	9/23 (39%)	6/16 (38%)	0.92

Mean (SD) compared with student's t-test with equal variances. Median [IQR] compared with Wilcoxon rank-sum for skewed variables. Number (%) compared with Fisher's exact test. Percentages represent percent of total column.

*indicates statistical significance after Bonferroni correction for multiple comparisons

[a]No patients had rapidly-progressive ILD during the study period (rapidly worsening symptoms over 3 months requiring oxygen or hospitalization) but several had a history of this presentation

DM: dermatomyositis, CADM: clinically amyopathic dermatomyositis, ILD: interstitial lung disease, PASP: pulmonary artery systolic pressure, DLCO: diffusion capacity for carbon monoxide, FVC: forced vital capacity, TLC: total lung capacity, CT: computed tomography

Table 2

Association between PFTs, pulmonary symptoms, and ILD among patients with abnormal PFTs and CT available for review

	No ILD (n = 24)	ILD (n = 15)	p-value[a]
PFT pattern			
Isolated low DLCO	11 (46%)	5 (44%)	0.52
Restriction	6 (25%)	6 (40%)	0.48
Obstruction	4 (17%)	0 (0%)	0.15
Mixed	0 (0%)	2 (13%)	0.14
Indeterminate	3 (12%)	2 (13%)	1.0
DLCO % predicted	70 [64, 78]	62 [54, 70]	0.06
FVC % predicted	81 [76, 96]	76 [68, 86]	0.08
TLC % predicted	90 [74, 99]	77 [72, 84]	0.02
Dyspnea	8 (33%)	10 (67%)	0.06
Cough	5 (21%)	5 (33%)	0.46
Neither	14 (58%)	5 (33%)	0.19

Median [IQR] compared with Wilcoxon rank-sum, Number (%) compared with Fisher's exact test.

[a]No p-values met statistical significance after Bonferroni correction for multiple comparisons.

PFT: pulmonary function tests, CT: computed tomography scan of the chest, ILD: interstitial lung disease, DLCO: diffusion capacity for carbon monoxide, FVC: forced vital capacity, TLC: total lung capacity