Pulmonary Function Tests in Systemic Sclerosis

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ABSTRACT

BACKGROUND

Respiratory system is the third commonest organ involved in Systemic Sclerosis (SSc), but may be silent without symptoms or chest X-ray abnormalities. Pulmonary Function Test (PFT) is a major tool for the investigation of lung involvement and measuring of breath (spirometry) is the most common of the PFTs. The objective of this study was to estimate the proportion of SSc patients having abnormal PFT.

METHODS

This was a hospital based cross sectional study conducted among 33 SSc patients to assess pulmonary involvement by chest X-ray and spirometry.

RESULTS

Abnormal PFT was observed in 63.6% patients and all of them had restrictive pattern PFT. Respiratory symptoms and signs were present in only 76.2% of patients with restrictive PFT and was absent in 23.8%, although they had restrictive PFT. X-ray evidence of Interstitial Lung Disease (ILD) was observed in 39.4% of patients and that of Pulmonary Hypertension (PH) in 6.1%. Chest X-ray was normal in 33.3% patients although they had abnormal PFT. 93.3% of patients with abnormal X-ray suggestive of ILD had restrictive PFT which was statistically significant. Only 61.9% of patients with restrictive PFT had X-ray features of ILD. Patients with restrictive disease had more respiratory symptoms and signs when compared with patients who had normal PFT.

CONCLUSIONS

PFT is a valuable screening tool for pulmonary involvement in all patients with SSc, since restrictive PFT and ILD can occur in SSc even in the absence of respiratory symptoms and signs or even when chest X-ray is normal.

KEYWORDS

Systemic Sclerosis, Pulmonary Function Tests, Spirometry, Interstitial Lung Disease, Restrictive PFT, Chest X-ray

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BACKGROUND

Systemic sclerosis (SSc) is a connective tissue disease characterized by varying degrees of fibrosis of skin and visceral organs.[1] The respiratory system involvement is the third most common organ involvement[2] in SSc and contributes to significant morbidity and mortality. Prevalence of pulmonary impairment has been reported to be as high as 57% to 86% in patients with SSc.[3] All aspects of the respiratory tract including the blood vessels, airways, pleura, parenchyma and musculature can be involved. Interstitial lung disease (ILD) is the most common pulmonary manifestation in SSc.[4]

Fibrotic and vascular pulmonary involvement including ILD and Pulmonary hypertension (PH) may shorten survival and are the leading causes of death accounting for 60% of early deaths in patients affected by SSc.[5] However, pulmonary involvement may often be silent, whereas skin fibrosis is usually the clinical feature drawing most attention.[6]

Recent studies have shown that pulmonary involvement and ILD is commonly seen in even 40% limited cutaneous SSc unlike previously thought to be more associated with diffuse cutaneous SSc.[7] Manifestations of ILD may range from asymptomatic to dyspnoea on exertion, non-productive cough, fine inspiratory Velcro crackles at lung bases and cor pulmonale. Others include aspiration pneumonia, alveolar haemorrhage, pleural involvement, small airway disease, malignancy, respiratory muscle weakness, spontaneous pneumothorax and silicosis.

Monitoring of pulmonary function and early detection of lung involvement is very crucial in management of SSc. Pulmonary function tests (PFT) are an important tool in the investigation and monitoring of patients with respiratory pathology relating to the large and small airways, the pulmonary parenchyma and the size and integrity of the pulmonary capillary bed. Although they do not provide a diagnosis per se, different patterns of abnormalities are seen in various respiratory diseases, which helps to establish a diagnosis.[8]

Different pulmonary function tests are available. Spirometry is the simplest of PFT to measure static lung volumes either, at rest which includes the slow (inspiratory or expiratory) vital capacity (sVC) and the forced vital capacity (FVC) or, the dynamic volumes which includes forced expiratory volume in 1 second (FEV1) and flow-volume loops.[9] Others like Diffusing capacity of the Lungs for Carbon monoxide (DLCO) along with FVC have been used traditionally to measure disease severity and reduction of both is associated with increased mortality due to ILD of SSc.[10] FVC is reduced in 40-75% of patients and DLCO in almost all patients and correlates with extent of lung disease on HRCT. [5] Studies about pulmonary manifestations of SSc in our setting are few. This study was undertaken with the primary aim of estimating the proportion of patients with SSc having abnormal PFT using spirometry.

METHODS

This study was a hospital based cross sectional study over a period of one year. All the patients, satisfying 2013 ACR/EULAR criteria for Systemic sclerosis who attended the Department of Dermatology during the study period were included in the study. Patients not willing for the study were excluded. Sample size of 17 was obtained by using the formula 'n' = 4PQ/l^2 where P is the prevalence of abnormal PFT in systemic sclerosis which is 85.8% according to a similar study conducted by Sharma et al in North India.[11] Q is 100-P. l is 20% of P**.** Consecutive sampling was done and 33 patients could be included in this study. Informed written consent was obtained from the participants and from the parent/guardian in case of children below 18 years. A structured questionnaire was used to record the medical history and details of examination of skin and respiratory system as well as investigation reports of the participants.

Chest X–ray and spirometry were done in all patients. When a patient performs a maximal inspiratory manoeuvre followed by a maximal expiratory one, it produces flow volume curves with positive expiratory and negative inspiratory limb which is charted on a graph. In restrictive lung disease, the expiratory limb has a convex or linear appearance because flow rates are preserved. Measurements that are made in spirometry include Forced Expiratory Volume in one second (FEV1), Forced Vital Capacity (FVC) and the ratio of the two volumes (FEV1/FVC).

Normal pattern
- FVC ≥ 80% predicted
- FEV1/FVC ≥70%

Restrictive pattern
- FVC < 80% predicted
- FEV1/FVC ≥ 70%
  - Mild Restriction: FVC 70-80%
  - Moderate Restriction: FVC 50-69%
  - Severe Restriction: FVC <50%

Obstructive pattern
- FEV1/FVC < 70%

Data was entered into Excel sheet and analysed in terms of descriptive statistics. The statistical method used was Chi-square test and a 'p' value <0.05 was taken as significant.

RESULTS

Among the 33 cases studied, maximum patients were in the 41-50 age group, the youngest being 12 years and the oldest being 63 years. Females outnumbered males (93.9%). The duration of the disease ranged from 1-5 years in 51.5% and 5-10 years in 27.2%. Most of the patients (22, 66.7%) had limited cutaneous SSc (lcSSc) while 11 (33.3%) had diffuse cutaneous SSc (dcSSc). Moderate degree of sclerosis of skin

was noted in 15 (45.5%) patients and 14 (42.4%) had only mild sclerosis based on Modified Rodnan Skin Score (MRSS). Three (9.1%) had severe sclerosis and one (3%) was in end-stage sclerosis.

Of the 33 patients, 20 (60.6%) patients had respiratory symptoms and all of them had dyspnoea while 13 (39.4%) of them also had dry cough associated with dyspnoea. Inspiratory crackles were heard in 10 (30.3%) patients.

Abnormal chest X-ray findings were seen in 15 (45.5%) patients. Among these, 13 (86.7%) patients had features of ILD in the form of reticulonodular opacities (11 patients), honeycombing and bi-basal fibrosis (1 patient each), forming 33.3%, 3.03% and 3.03% respectively of the total patients. Two (6.1%) patients had features of PH seen as enlargement of pulmonary artery and attenuation of peripheral pulmonary vascular markings. ILD was observed in 39.4% and PH in 6.1% of the total patients.

Mean FEV1 and FVC in this study population was 68.36±18.43 and 65.48± 19.46 respectively. Abnormal PFT was observed in 21 patients (63.6%) and all these patients had a restrictive pattern of PFT (Figure 1). Among these, moderate restriction was seen in 12 (57.1%); 5 (23.8%) had severe restriction and 4 (19.1%) had only mild restriction forming 36.4%, 15.2% and 12.1% respectively of the total study group. Comparison between patients with abnormal PFT (21 patients) and normal PFT (12 patients) was done and the following observations were made.

There was no significant difference with regard to age, sex and disease duration. (p value 0.161, 0.270, 0.172 respectively). Although restriction of PFT was more seen in dcSSc patients (82%) compared to only 55% of lcSSc, there was no statistical difference between dcSSc and lcSSc patients in terms of PFT abnormalities (p=0.125). And though 12 of the 21 patients with restrictive PFT (57.1%) had a moderate MRSS, MRSS did not have a statistically significant variation between patients with normal and restrictive PFT.

Among the 21 patients with abnormal PFT, respiratory symptoms and signs was present in only 16 (76.2%) patients, whereas 4 of the 12 (33.3%) patients with normal PFT also had dyspnoea or cough. Five (23.8%) patients, although they had abnormal PFT, did not have any respiratory signs and symptoms (Figure 2).

Cough was present in 11 (52.4%) of the 21 patients with restrictive PFT compared to 2 (16.7%) of the 12 patients with normal PFT. Conversely, among 13 patients who had cough, 11 (84.6%) had restrictive PFT, versus the 2 patients who had cough, but normal PFT and this was statistically significant (p=0.043).

Dyspnoea was present in 16 (76.2%) of the 21 patients with restrictive PFT, compared to 4 (33.3%) of the 12 patients who had normal PFT. Conversely, among the 20 patients with dyspnoea, 16 (80%) had restrictive PFT, versus 4 (20%) patients with normal PFT who had dyspnoea, and this was also statistically significant. (p= 0.015).

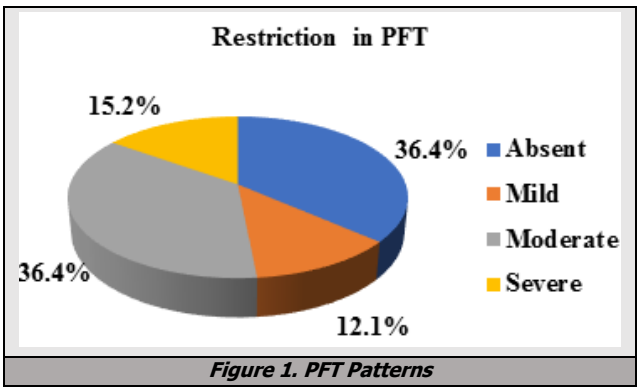

Figure 1. PFT Patterns

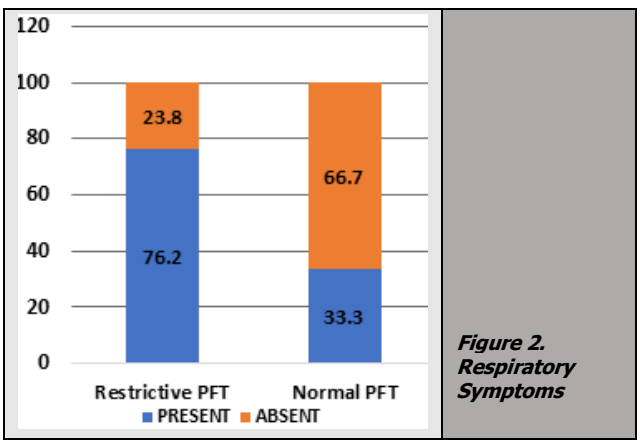

Figure 2. Respiratory Symptoms

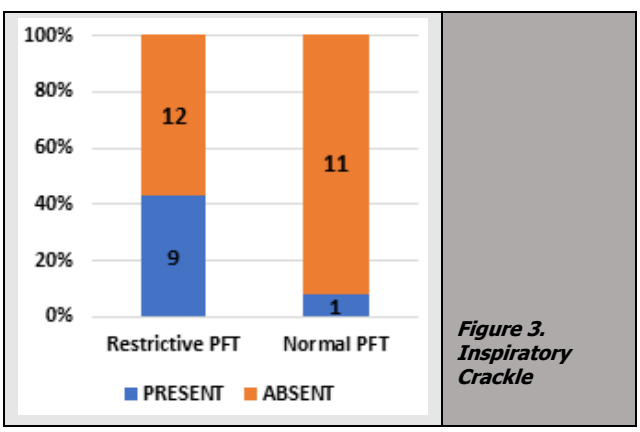

Figure 3. Inspiratory Crackle

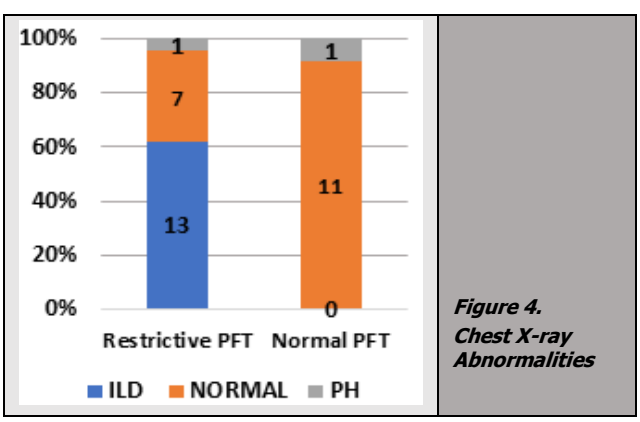

Figure 4. Chest X-ray Abnormalities

Inspiratory crackles were present in 9 (42.9%) of the 21 patients with restrictive PFT, compared to only one (8.3%) among the 12 patients with normal PFT. Of the 10 patients who had crackles, 9 (90%) had restrictive PFT versus one (10%) patient having crackles but a normal PFT. This was also statistically significant (p=0.038) (Figure 3).

So, SSc patients having cough, dyspnoea or inspiratory crackles have a high chance for restrictive PFT and ILD, highlighting the importance of history and clinical examination in these patients.

Among the 15 patients with abnormal chest X-ray, 14 (13 ILD & 1 PH) (93.3%) had restrictive PFT, and one had normal PFT in spite of evidence of PH. Chest X-ray features of ILD was seen on X-ray in 13 (61.9%) patients with restrictive PFT. PH was seen in one (4.8%) patient with restrictive PFT and also in one (8.3%) with normal PFT (Figure 4). There was significant statistical association between chest X-ray findings of ILD and restrictive pattern of PFT (p=0.002). SSc patients having chest X-ray abnormalities like reticulonodular shadows are most likely to show restrictive PFT pattern and ILD. In this study, 7 patients had normal chest X-ray, in spite of having restrictive PFT, indicating that chest X-ray is not a very sensitive tool in detection of ILD in SSc.

DISCUSSION

The mean age of 39.3±12.8 years in this study was similar to the study by Sharma et al in North India with 32.75±11.62 years.[11] Male to female ratio of this study was 1:15.5 compared to 1:7.8 in the study by Ferri et al[1] and 1:5.2 by Sharma et al.[11] Mean duration of disease was 4.7± 4.5 years. Ferri et al observed that mean duration of disease was 5.1 ±7.3 years.[1] Though the restriction of PFT was more in dcSSc in this study also, there was no statistical difference between dcSSC and lcSSc patients in terms of PFT abnormalities here, unlike most previous studies. Hafez et al had 43.3% patients with lcSSc and 56.7% with dcSSc.[12]

Dyspnoea was present in 60.6% of this study. Jezler et al observed dyspnoea in 65.5% patients, Sharma et al in 51.1% and Hafez et al in 93.3%.[2,11,12] Cough was present only in 39.4% in this study, while 53.3% had cough in the study by Hafez et al.[12] Inspiratory crackles were noted in 30.3% of this study but Hafez et al noted leathery crepitations in 80% while Jezler et al noted inspiratory crackles in only 15.5%.

Chest X-ray was abnormal in 45.5%, with 39.4% of them having features of ILD and 6.1% having features of PH. The most common finding was reticulonodular opacities in 33.3%, compared to 78.2% by Santos et al.[13] Pulmonary fibrosis on chest X-ray was seen in 19.1% by Steen et al.[14] Kane et al reported interstitial chest X-ray abnormalities in 44.9%.[15] Sharma et al reported abnormal chest X-ray in 65.3% with ground glass appearance (45.7%), reticular shadows (40%), honeycombing (10%), nodular opacity and paratracheal lymph nodes (4.2%).[11] Owens et al[16] observed pulmonary fibrosis in chest X-ray of 36% patients (37/104). Among them 70% (26/37) had reticulonodular shadows, 16% had reticular shadows and 14% had nodular opacities. Only 4% (4/104) had pulmonary artery enlargement in chest X-ray and all of them belonged to CREST variant of SSc.

Mean FEV1 of 68.36±18.43 and FVC of 65.48± 19.46 in this study was comparable to that of Hafez et al (mean FEV1 66.91 ± 16.13 and mean FVC 60.23 ± 12.02).[12] Mean FEV1/FVC was above normal (93.29 ± 11.44). Restrictive pattern of PFT was seen in all those with abnormal PFT (63.6%) in this study and by Hafez et al.[12] Sharma et al observed abnormal PFT in 85.8% patients.[11]

There was no significant difference as regards to age, gender and disease duration between dcSSc and lcSSc in comparison to patients with abnormal and normal PFT in this study or in the study by Hafez et al ($p > 0.05$).[12] A statistically significant correlation seen between pulmonary symptoms or signs (cough, dyspnea, inspiratory crackles) and restrictive lung disease in this study was observed by Steen et al also.[17] Jezler et al reported inspiratory crackles exclusively in the ILD patients, although in only 30% (p=0.001) but the presence of cough and dyspnoea did not vary between patients with and without ILD.[2]

All patients with features of ILD in chest X-ray belonged to restrictive PFT group. One patient with chest X-ray features of PH had restrictive PFT while the other had normal PFT. In the study by Steen et al, only 48% of patients with restrictive type of PFT had interstitial changes consistent with pulmonary fibrosis on chest roentgenogram.[17] In this study, 7 patients with restrictive PFT had normal chest X-ray, indicating that chest X-ray is not very sensitive in detection of ILD in SSc.

CONCLUSIONS

Abnormal PFT was observed in 63.6% of the SSc patients and all of them had restrictive pattern with significant association to cough, dyspnoea and inspiratory crackles as well as chest X-ray findings of ILD. However, 23.8% patients did not have any pulmonary symptoms or signs in spite of having restrictive PFT. Also, 33.3% of the patients with restrictive PFT had normal chest X-ray indicating that chest X-ray is less sensitive than PFT in detection of ILD in SSc. Conversely, one patient with X-ray features of PH had normal PFT.

So, the absence of respiratory symptoms or signs and even a normal chest X-ray in SSc patients does not preclude a restrictive PFT and therefore ILD. This highlights the importance of PFT as an initial screening tool for ILD in SSc. It is advisable to do PFT in all patients with SSc, to detect early pulmonary involvement and together with chest X-ray will be ideal when facilities like HRCT are not available.

REFERENCES

[1] Ferri C, Valentini G, Cozzi F, et al. Systemic sclerosis: demographic, clinical, and serologic features and survival in 1,012 Italian patients. Medicine (Baltimore) 2002;81(2):139-153.

[2] Jezler SF, Santiago MB, Andrade TL, et al. Interstitial lung disease in patients with progressive systemic sclerosis: a study of 58 cases. J Bras Pneumol 2005;31(4):300-306.

[3] Marie I, Dominique S, Levesque H, et al. Esophageal involvement and pulmonary manifestations in systemic sclerosis. Arthritis Care Res 2001;45(4):346-354.
[4] Nadkar MY, Desai NK. Lung involvement in systemic sclerosis. Med Update 2011:298-299.
[5] Solomon JJ, Olson AL, Fischer A, et al. Scleroderma lung disease. Eur Respir Rev 2013;22(127):6-19.
[6] Morelli S, Barbieri C, Sgreccia A, et al. Relationship between cutaneous and pulmonary involvement in systemic sclerosis. J Rheumatol 1997;24(1):81-85.
[7] Strollo D, Goldin J. Imaging lung disease in systemic sclerosis. Curr Rheumatol Rep 2010;12(2):156-161.
[8] Ranu H, Wilde M, Madden B. Pulmonary function tests. Ulster Med J 2011;80(2):84-90.
[9] Behr J, Furst DE. Pulmonary function tests. Rheumatology 2008;47(Suppl 5):65-67.
[10] Goh NSL, Desai SR, Veeraraghavan S, et al. Interstitial lung disease in systemic sclerosis: a simple staging system. Am J Respir Crit Care Med 2008;177(11):1248-1254.
[11] Sharma VK, Trilokraj T, Khaitan BK, et al. Profile of systemic sclerosis in a tertiary care center in North India. Indian J Dermatol Venereol Leprol 2006;72(6):416-420.
[12] Hafez EA, Hamza SH, Morad CS, et al. Pulmonary manifestations in Egyptian patients with systemic sclerosis. The Egyptian Rheumatologist 2017;40(1):1-6.
[13] Santos MK, Faria FB. Pulmonary involvement in systemic sclerosis: cases review. Radiol Bras 2006;39(3):181-184.
[14] Steen VD, Conte C, Owens GR, et al. Severe restrictive lung disease in systemic sclerosis. Arthritis Rheum 1994;37(9):1283-1289.
[15] Kane GC, Varga J, Conant EF, et al. Lung involvement in systemic sclerosis (scleroderma): relation to classification based on extent of skin involvement or autoantibody status. Respir Med 1996;90(4):223-230.
[16] Owens GR, Fino GJ, Herbert DL, et al. Pulmonary function in progressive systemic sclerosis. Comparison of CREST syndrome variant with diffuse scleroderma. Chest 1983;84(5):546-550.
[17] Steen VD, Owens GR, Fino GJ, et al. Pulmonary involvement in systemic sclerosis (scleroderma). Arthritis Rheum 1985;28(7):759-767.