Measurement of diffusion lung capacity (DLCO) in silicosis patients: Correlation with radiographic abnormalities on high-resolution CT scan chest

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ABSTRACT

Objective: This study was conducted to evaluate diffusion capacity of lung for carbon monoxide (DLCO) in patients with simple and complicated silicosis and to correlate abnormal findings detected, if any, with the computed tomography abnormalities in these patients. Methods: This study included 56 patients with simple and complicated silicosis and without tuberculosis, in whom we performed DLCO as per standard technique. Various computed tomography findings, that is, presence, size and distribution of nodules associated with relative parenchymal and vascular markings, were recorded in the study subjects and classified into standard grading to be finally compared with DLCO. Visual grading score system was used to describe the extent of emphysematous changes based on the area of abnormally low attenuation, vascular disruption, bullae and so on and data were recorded. Results: Results showed that 85.7% patients had small opacities of varying grades and 28.5% showed large opacities, with 16% of them having type ‘C’ large opacities. The mean DLCO (% predicted) of patients with category ‘0’ high-resolution computed tomography (HRCT) abnormality was 92.3 ± 6.8 (within normal limits), and this gradually decreased with increasing HRCT category to 44.2 ± 11.2 in grade ‘4’ of progressive massive fibrosis (PMF) patients in this study (P < 0.01). This reflects a significant inverse correlation between visual HRCT category and the DLCO % predicted (r = −0.89, P < 0.001). The mean DLCO (% predicted) was 51 ± 12.6 in patients with grade ‘1’ emphysema in HRCT, 53 ± 13.5 in grade ‘2’, 43 ± 6.4 in grade ‘3’ and 37.7 ± 6.3 in grade ‘4’; however, there was no correlation between emphysema grading and pulmonary functional index (r = −0.33, P = 0.15). Conclusion: This study observed significant abnormality in DLCO among silicosis patients and its strong correlation with the extent of radiological abnormality. HRCT finding of large opacities could be an important indicator of the severity of silicosis, as reflected by significantly reduced DLCO in such patients.

KEY WORDS: Diffusion Lung Capacity (DLCO), HRCT scan chest, silicosis

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Submitted: 15-May-2021 Revised: 21-May-2022 Accepted: 31-May-2022 Published: 01-Jul-2022

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How to cite this article: Dixit R, Jalutharia J, Gupta A, Mathur R, Goyal M, Gupta N, et al. Measurement of diffusion lung capacity (DLCO) in silicosis patients: Correlation with radiographic abnormalities on high-resolution CT scan chest. Lung India 2022;39:352-6.
INTRODUCTION

Silicosis is a potentially fatal, irreversible, fibrotic pulmonary disease that may develop subsequent to the inhalation of large amounts of silica dust over time and is one of the most important occupational diseases worldwide. According to the current guidelines of the International Labor Organization (ILO), the principal method of diagnosing silicosis is by the analysis of chest X-rays and history of occupational exposure to silica dust. On the basis of different exposure intensities, latency periods and natural histories, silicosis has been well characterised as chronic, accelerated and acute form. The chronic or classic form usually follows 10 or more years of exposure to silica-containing dust. Accelerated silicosis results from heavy exposures and develops more rapidly than the chronic form, often with a latency of 5–10 years, and gradually progresses inexorably even after the exposure is interrupted. The acute form of silicosis is a consequence of exposure to high level of respirable dust, usually from months up to 5 years, and the clinical course is one of rapid progression.

Pulmonary function tests, although not used as diagnostic tools, are widely employed in longitudinal studies of individuals with silicosis to assess functional impairment in these patients. The single-breath diffusion capacity of lungs for carbon monoxide (DLCO) is the clinically most useful pulmonary function test after spirometry and lung volumes. Several studies have demonstrated pulmonary function abnormalities in patients having different forms of radiographic lesions following occupational exposure to crystalline silica. High prevalence of dyspnoea, restrictive impairment of lung function and impaired diffusion capacity have been reported in patients having simple or complicated silicosis. The reduced level of lung functions in silicosis patients also correlates with abnormal radiological findings on computed tomography (CT) scan. Since imaging and function tests are the most widely used diagnostic resources in the follow-up evaluation of individuals with silicosis, it is fundamental to establish the correlation between these two. The aim of this study was to analyse different grades of radiological abnormality on high-resolution computed tomography (HRCT) scan thorax among silicosis patients and measure functional derangements if any by measuring DLCO in each of them. The study was conducted to find out the correlation, if any, between DLCO and severity of radiological abnormality on HRCT scan chest among silicosis patients.

MATERIALS AND METHODS

This study was a cross-sectional descriptive study conducted among the patients with history of occupational exposure to silica dust and radiologically confirmed silicosis. Sample size was calculated at 95% confidence interval using appropriate statistical formulas. The method of sampling was convenient. Patients having silico-tuberculosis and current smokers were not included in this study. Fifty-six subjects constituted the final study population. Participants were informed regarding the objective of the study and written informed consent was taken from them. The study protocol was approved by the institutional ethical research committee.

All patients underwent spirometry using RMS Helicos 401 spirometer attached to a computer and readings were interpreted based on the American Thoracic Society/European Respiratory Society (ATS/ERS) guidelines. DLCO was measured by single-breath hold technique (Quark Body Box System; COSMED Srl, Rome, Italy) by following standard procedural steps. While testing for DLCO, the manoeuvre was demonstrated and explained to each study patient. The patient was seated for at least 5 min before the procedure was started and remained seated throughout the procedure. The subject then breathed quietly while he/she was connected to the instrument. The subject then exhaled to residual volume. At residual volume, the subject’s mouthpiece was connected to the source of the test gas and the subject was instructed to inhale to total lung capacity. After inspiring the test gas, the subject held the breath for 10 s and then exhaled smoothly and rapidly without interruption, but without maximum force. The readings were interpreted based on the ATS/ERS guidelines. The results of this measurement were reported as DLCO. The diffusion coefficient (Kco) was calculated from DLCO by dividing it by volume ventilated (VA) that more specifically represents diffusion.

HRCT of thorax was performed with MX 16 CT scanner (Philips, Cambridge, MA, USA) using volumetric acquisition with filter back projection for reconstruction of images. The algorithm used was multidetector (MD) CT with 16 rows of detectors with a slice thickness of 0.5 mm and slice interval of 0.5 mm. An automatic processor ‘Fuji film dry pix 7000’ was designed to develop the HRCT film. All thoracic scans were obtained without contrast medium. A standard CT scan grading system for silicosis was utilised in these patients based on the presence, size and distribution of nodules and relative parenchymal and vascular markings. Category ‘0’ was given if there were no definite nodules. Category ‘1’ was given if small number of nodules were detected with no disruption of vascular markings. Category ‘2’ indicated the presence of many nodules, but with no confluence and with visible normal parenchymal markings. Category ‘3’ CT scans abnormality demonstrated confluence of nodules, usually associated with disruption of vascular markings. Category ‘4’ was given for confluence of nodules extending over two or more slices, consistent with the diagnosis of progressive massive fibrosis (PMF).

The visual grading score system to describe the extent of emphysematous changes in patients of silicosis based on area of abnormally low attenuation, vascular disruption or bullae, and so on was also performed in each study.
subject. In this, grade ‘1’ was given if less than 25% of the lung parenchyma was involved, grade ‘2’ if 25%–50% of the parenchyma demonstrated emphysematous changes, grade ‘3’ if 50%–75% of the area was abnormal and grade ‘4’ if more than 75% of the lung parenchyma was affected by emphysematous changes.

The data were analysed and statically evaluated using Statistical Package for the Social Sciences (SPSS) software, version 20 (IBM Corp., Armonk, New York, USA). Quantitative data were expressed as mean and standard deviation while qualitative data were expressed in percentage. Difference of mean between more than two groups was tested by Kruskal–Wallis H test followed by post hoc test, that is, Dunn’s test if required. $P$ value less than 0.05 was considered statistically significant.

RESULTS

Fifty-six confirmed silicosis patients were analysed in this study as per the protocol. Most patients were male ($n = 52$, 92.8%) with a mean age of 43.1 ± 10.8 (age range 27–68) years. More than half of the subjects ($n = 35$, 62.5%) were non-smokers and 37.5% ($n = 21$) were ex-smokers. Majority of the patients were engaged with stone cutting work ($n = 21$, 37.5%), followed by stone grinding ($n = 7$, 12.5%), well digging ($n = 6$, 10.7%) and others.

Spirometry revealed a forced vital capacity (FVC) of 70.2% predicted (range 28–104, standard deviation [SD] 21.2), forced expiratory volume in first second (FEV1) of 65.7% predicted (range 22–106, SD 22.3) and FEV1/FVC% of 73.4% predicted (range 52–101, SD 12.8). Spirometry revealed a mixed pattern of abnormality in maximum cases (46.4%), followed by restrictive pattern (19.6%) and obstructive pattern (14.2%). Spirometry was normal in 19.6% cases.

The absolute mean DLCO was 12.2 ml/min/mmHg (range 2.2–23.6 ml/min/mmHg, SD 7.5; 95% confidence interval [CI]: 2.2 ± 3.7) (±10.4%). The mean DLCO (%) predicted value was 63.6 ± 18.3 (range 10%–94%). The mean DLCO (%) predicted value in acute silicosis was 61.2 ± 27.5, in accelerated silicosis was 71.6 ± 16.0 and in chronic silicosis was 60.8 ± 18.1. The absolute mean $V_A$ was 2.2 l (range 0.7–3.7 l, SD 0.7; 95% CI: 2.2 ± 0.3) (±17.5%).

The mean DLCO (%) predicted) of patients with HRCT grade 0 was 92.3 ± 6.8, that is, within normal limits, and it gradually decreased with increasing HRCT grading to 84.8 ± 6.8 in category 1, 76.4 ± 7.3 in category 2, 61.2 ± 10.1 in category 3 and to 44.2 ± 11.2 in CT category 4 (PMF patients) in our study ($P < 0.01$) [Table 1].

The mean DLCO (%) predicted was 51 ± 12.6 in patients with grade 1 emphysema in HRCT, 53 ± 13.5 in grade 2, 43 ± 6.4 in grade 3 and 37.7 ± 6.3 in grade 4.

The distribution of individuals according to HRCT abnormalities as per the CT grading of silicosis was as follows: six (10.7%) in category 0, seven (12.3%) in category 1, 13 (23.2%) in category 2, 11 (19.6%) in category 3 and 19 (33.9%) in category 4. Figure 1a–e shows different grades of CT abnormality in silicosis patients in this study. Emphysematous changes were also observed in 15 (26.7%) subjects according to the HRCT grading system. Distribution of individuals according to the HRCT emphysema abnormalities as per the CT grading of silicosis was as follows: six (40%) in grade 1, four (26.6%) in grade 2, three (20%) in grade 3, and two (13.3%) in grade 4.

Table 2 shows significant inverse correlations between visual HRCT category and the DLCO % predicted ($r > −0.8$, $P < 0.001$); however, there was no significant correlation between emphysema grading and DLCO values ($r$ value = −0.3, $P = 0.15$).

DISCUSSION

Several studies have been done in silicosis patients to analyse the correlation between lung functions and radiological abnormalities. Both obstructive and restrictive patterns are reported regardless of the smoking status, with a low profusion category in simple silicosis and an increased prevalence of restrictive changes with increased profusion. After controlling for age, smoking and duration of exposure to silica, a statistically significant increased risk of obstructive and mixed changes was seen with PMF by Rosenman et al.[9] The presence of emphysema in silicosis is believed to be secondary to the development of PMF, even in the absence of smoking. Kinsella et al.[9] observed the degree of emphysema rather than the degree of silicosis that determines the level of pulmonary functions. A high prevalence (46%) of restrictive pattern (vital capacity <80% predicted) was detected in simple silicosis by Koskinen et al.[8] They also observed 47% patients having abnormal DLCO in simple silicosis and more impaired DLCO in advanced simple silicosis (65% of

### Table 1: DLCO (predicted) values in silicosis patients as per their HRCT grade abnormalities

| Parameter | HRCT grading | $P$ |
|-----------|--------------|-----|
| Mean DLCO | 92.3±6.8     | 84.8±6.8 | 76.4±7.3 | 61.2±10.1 | 44.2±11.2 | <0.01 |

**DLCO**= diffusion capacity of lung for carbon monoxide, **HRCT**= high-resolution computed tomography

### Table 2: Pearson’s correlation coefficients for the correlations between DLCO and results of the scores obtained with HRCT abnormalities

| Functional index | HRCT grading | Emphysema grading |
|------------------|--------------|-------------------|
| DLCO             | $r = -0.89$  | $-0.33$           |
| $P$              | <0.01        | 0.15              |

**DLCO**= diffusion capacity of lung for carbon monoxide, **HRCT**= high-resolution computed tomography
predicted in category 3 compared to 85% of predicted in category 1), suggesting DLCO as a sensitive tool to assess lung functions. Results of most studies including ours suggest that simple silicosis (category 0, 1) does not produce significant impairment in lung function; however, impairment in lung function on spirometry or DLCO or a combination of these two was observed in patients with advanced simple silicosis (category 3).

A major advantage of HRCT is that it offers additional information for early detection of small opacities and emphysematous changes with identification of complications.\[10] Description of the CT appearance of silicosis in radiological literature has been limited.\[4] The advantage of decreased superimposition of parenchymal structures provided by using thin CT slices in the transaxial plane allows clear visualisation of the distribution and severity of parenchymal changes.\[11] CT scan is superior to chest radiograph in evaluation of silicosis, with its major advantage being ability to detect parenchymal destruction. The presence of a significant relation between the profusion of the parenchymal opacities evaluated by HRCT and the DLCO has not been extensively reported in previous studies. Results of our study suggest that, in patients presenting with large opacities, there is a progressive decrease in DLCO with increasing extent of radiological abnormality on HRCT ($r > -0.8, P < 0.001$).

The pathophysiology of silicosis involves interaction between the pulmonary alveolar macrophage and silica particles. The release of chemotactic and inflammatory mediators results in recruitment of other polymorphonuclear cells and additional macrophages. The result of this cascade leads to chronic lung inflammation and eventually fibrosis.\[12] Therefore, we observed compromised DLCO reflecting increased pulmonary vasculature architecture distortion in category 3 and 4 HRCT, when compared to category 0 and 1 HRCT chest grading.

The mean DLCO (% predicted) among silicosis patients gradually decreased with increasing HRCT grading from $84.6 \pm 6.9$ in category 1 to $76.3 \pm 7.3$ in category 2 and from $61.0 \pm 10.2$ in category 3 to $44.1 \pm 11.1$ in CT category 4 (PMF patients) in our study ($P < 0.01$). A study done by Talini et al.\[13] also showed that, the increasing severity in HRCT categories is associated with progressive deterioration in diffusion capacity of the lung. The change in mean TLco (diffusion capacity of carbon monoxide using single breath) was from $116.5 \pm 30.4$ in category 0 to $78.8 \pm 40$ in category ≥2. In another study from Brazil by Antão et al.,\[14] the large opacities were associated with significantly lower mean values for DLCO (% predicted) in the group of workers with silicosis (only 11% patients had reduced DLCO <75% predicted in HRCT category 0 when compared with HRCT category ≥2 [26% patients]). Lopes et al.\[15] observed the mean DLCO (% predicted) changing from $67.8 \pm 17.2$ in category 1 (small opacities) to $61.8 \pm 18.7$ in patients with PMF on HRCT ($P = 0.019$). Studies by Arakawa et al.,\[16] Ooi et al.,\[17] and Kinsella et al.\[9] also reported significantly reduced diffusion capacity in the presence of complicated silicosis. The results of the present study and all other studies suggest that functional abnormality of lungs correlates more strongly with the extent of large opacities than with small opacities. Therefore, HRCT finding of large opacities can be an important indicator of the severity of silicosis and decreased DLCO.

In the present study, we could not find any correlation between emphysema grading and pulmonary functional index; however, Bergin et al.\[6] observed significant correlation between the visual CT emphysema score and the DLCO % predicted ($r > 0.7, P < 0.001$). This difference might be due to small sample size in the study of Bergin et al. ($n = 17$) compared to the present study ($n = 56$). Secondly, in both studies, visual scoring system was used for grading emphysema in HRCT, which may be associated with inter-observer variation. More so, there may be gradual changes in emphysema grading on HRCT.

![Figure 1](image-url)
that may not be associated with significant DLCO changes at point of time. In silicosis, more severe disease reflects two pathological states, that is, fibrosis causing restrictive changes and secondly, the development of secondary emphysema due to fibrosis causing hyperinflation and decreased air flow. Both increasing fibrosis of lung and emphysematous changes are inversely related with diffusion capacity of lungs.

To summarise, this study categorised silicosis patients on the basis of nodules and emphysematous changes on HRCT chest into different grades of abnormalities. DLCO (% predicted) was also calculated in each patient for individual grading of HRCT abnormality, where we observed a good correlation between the CT assessment and DLCO. The decreased value of diffusion capacity of lung reflects compromised lung function in patients with silicosis, that correlates well with the extent of the profusion of nodules on radiological assessment. Since HRCT is superior to conventional chest radiograph and we observed good correlation between changes in DLCO value and changes in HRCT grading, we conclude that HRCT chest is the most sensitive tool to assess deterioration in DLCO at the earliest. This study also suggests that functional damage of lungs correlates more strongly with the extent of larger opacities compared to small opacities. HRCT finding of large opacities could be an important indicator of the severity of silicosis, as reflected by decreased diffusion capacity of lung in such patients.

Declaration of patient consent
The authors certify that they have obtained all appropriate patient consent forms. In the form, the patients have given their consent for their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published, and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Financial support and sponsorship
Nil.

Conflicts of interest
There are no conflicts of interest.

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