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Technegas ventilation SPECT for evaluating silicosis in comparison with computed tomography

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To compare the subtle pulmonary parenchymal morphologic changes with ventilation function in patients with silicosis, the conventional CT, high resolution CT and technegas ventilation SPECT were performed. In 25 silicotic patients and six controls, the pulmonary ventilation state was evaluated by an index called the coefficient of variation (CV), which expresses the subliminal heterogeneous distribution of technegas in the lungs. The results showed that with silicosis the CV value is significantly higher than that without silicosis. The CV value was proved by multifactorial analysis to independently reflect the extent of the appearance of small scattered interstitial findings such as nodules, septal thickening and bulla, which were typical findings for silicosis. The CV value calculated from the technegas SPECT correlated well with the severity of silicosis. It is considered that the CV value can also express the functional state of the silicotic lung.

Key words: technegas, SPECT, computed tomography, silicosis

INTRODUCTION

ESTIMATION of disease severity in silicosis generally involves a combination of chest radiography and pulmonary function test. The chest radiography is used to detect the characteristic pulmonary parenchymal and interstitial changes, but a previous report[1] has suggested that an abnormal decrease in ventilation capacity preceded abnormal findings on chest radiographs in pneumoconiosis. Another pathological study[2] documented autopsy findings of fibrotic lesions and silicotic nodules in workers who had normal premortem chest radiographs. These results suggest that the chest radiographs may tend to ignore the early subtle lesions and do not have a good correlation with the extent of impairment of pulmonary function. The morphologic changes in silicosis have recently been evaluated by computed tomography (CT) in some studies,[3–6] and CT has been proved superior to chest radiography in the early detection of pulmonary nodules and interstitial changes. Studies on the relationships between the CT findings and lung function in silicotic patients, however, were limited and contradictory.[7–9] In this study, we use technegas[10] to evaluate the functional state of silicosis. Since almost all interstitial lesions such as nodule, bulla and septal thickening are subliminal under the FWHM of the SPECT, we hypothesize that the distribution of technegas can represent some pathologic process of diffuse lung diseases, resulting in a heterogeneous distribution pattern. We decided to measure the heterogeneity of technegas distribution in silicotic lungs, and compare it with findings in the corresponding CT image.

MATERIALS AND METHODS

Patients

Twenty-five patients with silicosis and six normal volunteers, as controls, were studied by means of the same examination protocol. The diagnosis of silicosis was based on a definite history of exposure to silica dust and silicotic findings on chest radiography according to the 1980 International Labour Office (ILO) Classification of Radiographs of Pneumoconioses.[11] The ten patients had worked in a zinc mine for an average of 20 years with a

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range of 4–44 years, and fifteen patients had worked at tunnel construction for an average of 16 years with a range of 8–25 years. The mean age of the patients was 55 years with a range of 49–72 years, and the mean age of the controls was 50 years with a range of 33–62 years. All patients were ex-smokers except for one current smoker. Four of six volunteers were ex-smokers and two were non-smokers.

Ventilation scintigraphy

Technegas was produced in the usual way[10] with a commercially available technegas generator (Tetley Technologies). 266–600 MBq of ^{99m}Tc-pertechnetate in 0.1 m*l* was loaded twice into a graphite crucible to increase the radioactivity. Technegas was administered through a mouthpiece, with a nose clip *in situ*, to the patients who were in the sitting position. The patients slowly inhaled and then held their breath for 5 seconds at the maximal point of inspiration. This procedure was repeated three to five times. Following conventional planar images in anterior, posterior, right and left lateral views, SPECT was obtained with a three head gamma-camera (TOSHIBA, GCA9300/HG) equipped with a high-resolution, low-energy collimator. Counts of one view were acquired in the form of a 128 × 128 matrix in 50 seconds. The FWHM of the SPECT was approximately 14 mm. Slice thickness was 9.6 mm. The appropriate Butterworth filter value was chosen by a phantom study. The phantom consisted of a flood source containing many plastic cylinders 4, 6, 8 and 10 mm in diameter which simulated scattered subliminal defects. On the basis of the phantom studies, a Butterworth filter with a range of 0.1 to 0.15 was selected, in which subliminal distribution of small defects were not obscured by a smoothing effect in the low band field and statistical noise was not amplified in the high band field. Finally, a filter value of 0.13 was applied to every reconstruction in this study.

CT evaluation

All CT scans were performed on a GE9800 (General Electrics) scanner. Conventional CT (CCT) scans were obtained with 10 mm section thickness at 1 cm intervals from the apex to the base of the lung and five to seven high resolution CT (HRCT) scans were subsequently obtained with 1.5 mm section thickness through the upper, middle and lower thorax. Both CCT and HRCT scans were reviewed at window values most appropriate for pulmonary parenchyma (window value −500 to −700 and window width 1000 to 2000). Imaging was performed while patients were supine and holding their breath at maximal inspiration.

For CT images, three zones of the thorax were chosen for evaluation. The three zones were defined as follows: the upper zones are at the level of the aortic arch, the middle zones at the level of the carina, and the lower zones at a level of 2 cm above the dome of the right hemidiaphragm. By using this method, six regions can be obtained in the right and left lungs for every patient. Finally, a total of 186 regions for the 25 patients and six controls were obtained for analysis of findings in CT images.

The profusion of parenchymal opacities seen on the selected CT scans were graded by the principle which Begin[3] reported. The absence of opacities was classified as grade one (0/–, 0/0, 0/1). Definite presence of opacities without obliterating the vascular markings was classified as grade two (1/0, 1/1, 1/2). If the opacities were slightly obliterating the vascular markings, they were classified as grade three (2/1, 2/2, 2/3). For the most severe blunting of the vascular markings, the opacities were classified as grade four (3/2, 3/3, 3/+). No case in our study was classified as grade four. Other findings, such as emphysema, bulla, honeycomb and septal thickening of the secondary lobule were also evaluated by visually estimating the extent in each selected image. The extent score was defined as the percentage of lung parenchyma that showed evidence of each recorded finding: 1, involvement of less than 25% of the image, 2, 25%–50%, and 3, more than 75%.

Selection of the same axial section between CT and SPECT

To compare the CT image and that of SPECT on the same level, a marker was made by crossing two catheters obliquely, which was put on the surface of the chest of the patient when CT or SPECT was performed. Before the SPECT examination, the two catheters were filled with some solution at a low ^{99m}Tc concentration. According to the distance between the two catheters, the same axial section of CT and SPECT was selected.

Measurement of the heterogeneity of technegas distribution

On the SPECT image, the lung regions corresponding to the CT were selected to measure the heterogeneity of technegas distribution. Two cases were excluded from this study because they had marked deposition of technegas in the central bronchial tract. Finally, a total of 174 regions for the 23 patients and six controls were obtained. Peripheral lung areas were chosen for study to avoid large vessels in the central lung. To fix the outer contour of the lung, the peripheral parts of the lung with a low count about 20% or less of the maximal pixel radioactivity were cut off automatically. A ROI with a size of 10 × 10 pixels, which is maximized to encompass as much lung with typical silicotic lesions as possible, was set for each of these regions. In controls and patients without findings of silicosis (0/–, 0/0, 0/1), a ROI was set in the dorsal part of both lungs that are predisposed to silicosis.[12]

The coefficient of variation (CV) in each ROI was employed for the quantitative analysis to evaluate the heterogeneity of the technegas distribution. The CV was

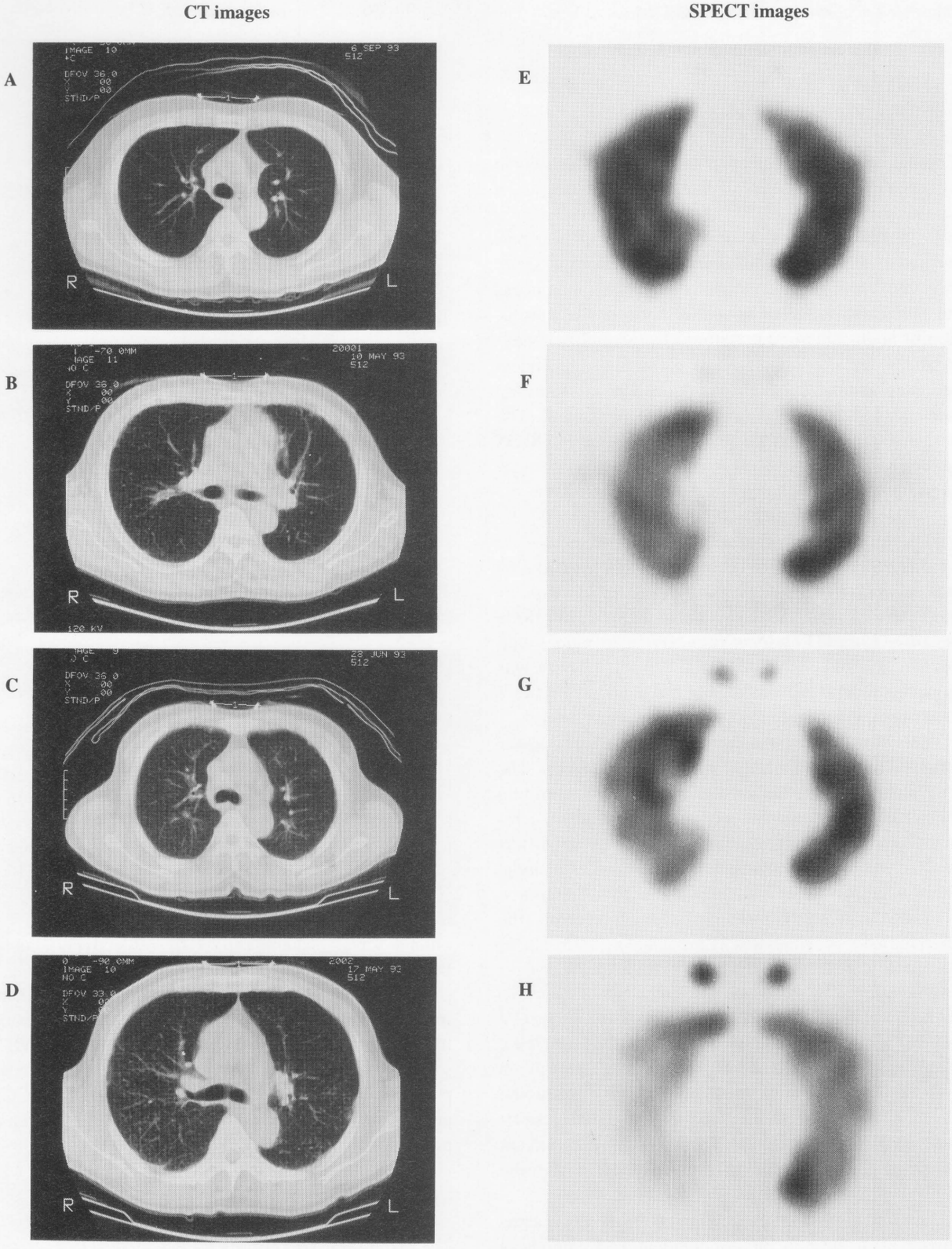

Fig. 1 Image A to D are the images of CT and E to H are the images of ventilation SPECT. Both CT and SPECT images are obtained at same axial section. A and E are the images of control. B–D and F–H are the images of grade 1 to grade 3 of silicosis. Corresponding to the CT grade, the distribution of technegas is homogeneous in controls and becomes heterogeneous with the degree of silicotic lesion.

calculated according to the formula below.

$$CV = \frac{\sqrt{\frac{\Sigma(X-\bar{X})^2}{n-1}}}{\bar{X}} \times 100\%$$

X in the above formula means the count of radioactivity in each pixel, $\bar{X}$ means the mean pixel activity of ROI, and n means the number of pixels.

Comparison of the CV means in the groups was performed by the two-tailed unpaired Student's t-test. Stepwise multiple regression analysis was used to assess the correlation between CV and CT findings when profusion of nodules, emphysematous change, bulla, honeycomb and septal thickening were adopted as independent variables, and the CV value as a dependent variable. A p value less than 0.05 was regarded as significant. The statistical analysis was made by means of the PC SPSS system.

RESULTS

Among 138 regions of silicotic patients, 28 (20.3%) regions were classified as grade one, 72 (52.2%) regions as grade two, and 38 (27.5%) regions as grade three according to the CT findings, respectively. In regions with silicotic lesions, the distribution of radioactivity was more heterogeneous than that of the controls. Figure 1 shows typical CT and SPECT images of each grade.

There were 46 regions for upper, middle and lower zones of the lungs of silicotic patients, respectively. The CV value for upper zones was 28.5 ± 4.3(%), middle zones 28.9 ± 5.2(%), and lower zones 29.3 ± 4.9(%), respectively. There was not a statistically significant difference ($p > 0.05$) in CV values among the zones of the lung. There was also no statistically significant difference ($p > 0.05$) between the zones of the lung of controls (the CV value for upper zones was 21.8 ± 2.8(%), 22.9 ± 4.2(%) for middle zones, and 22.0 ± 3.3 (%) for lower zones, respectively).

The CV value for controls was 22.2 ± 3.1(%). The CV value for regions classified as grade one was 27.1 ± 6.7(%), 31.0 ± 7.9(%) for grade two, and 34.3 ± 6.7(%) for grade three, respectively. In regions with nodular opacity, the CV value was much greater than for those with no evidence of a nodule ($p < 0.001$). There was also a significant difference between the different grades of regions ($p < 0.05$) (Fig. 2).

The relationship between CV and CT findings is summarized in the Table 1. Besides nodules, emphysema was found in 62 regions (44.9%). CV of regions with emphysematous change was much greater than those without emphysema ($p < 0.001$). There were 28 regions with bulla (20.3%), 36 regions with thickening of secondary lobular septa (26.1%), and 5 regions with honeycomb (3.6%). The CV value was significantly greater in regions with bulla or septal thickening ($p < 0.01$, respectively), but not in regions with honeycomb ($p > 0.05$).

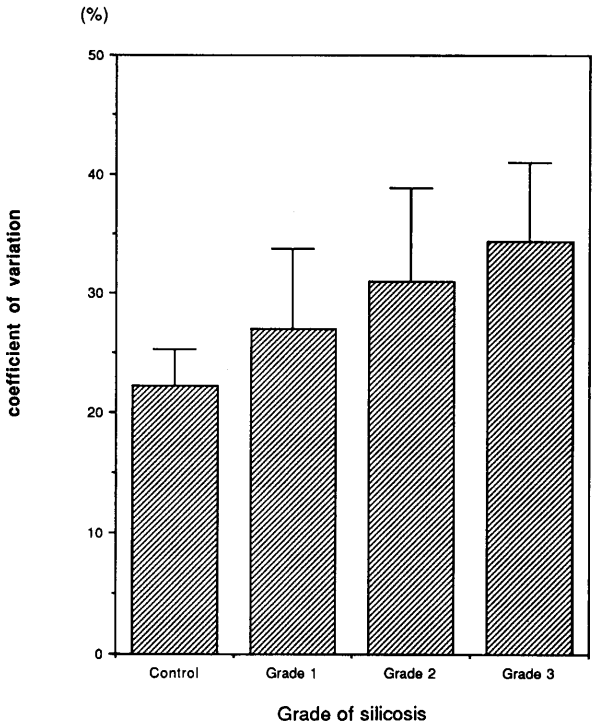

Fig. 2 Coefficient of variation obtained from SPECT image in the various groups according to CT grading. Values are averages ± 1SD.

Table 1 The value of coefficient of variation in regions with or without silicotic findings on CT

Findings	CV in regions with findings	CV in regions without findings	p value
Emphysema	34.62 ± 7.83	27.96 ± 6.08	0.001
Bulla	37.25 ± 8.44	30.35 ± 5.96	0.006
Septal line	36.39 ± 8.82	29.28 ± 6.92	0.008
Honeycomb	29.00 ± 2.24	31.39 ± 7.72	0.08

A stepwise regression model was constructed to examine the relationships between the CV value and the extent of CT findings on CCT and HRCT. In this analysis, the CV value was independently and positively related to the profusion of nodules, bulla and septal thickening on CCT, and independently and positively related to profusion of nodules and bulla on HRCT (Table 2).

DISCUSSION

The current standard criteria for the diagnosis of silicosis are based on the history of silica exposure, chest radiography, pulmonary function tests, and histopathologic findings for the lung when available. Though the ILO standard for interpretating chest radiographs is the generally used "gold standard" for silicosis extent, some subclinical fibrotic changes may tend to be ignored.[2,13]

Table 2 Relationships between the value of coefficient of variation and findings on conventional computed tomography and high resolution CT from stepwise multiple regression analysis

Findings	Standard coefficient (CCT)	Standard coefficient (HRCT)
Profusion of nodules	0.349*	0.381*
Bulla	0.305*	0.339*
Emphysematous change	0.010†	0.101†
Septal thickening	0.228*	0.190†

* $p < 0.0001$
† Not significant

Recently, many studies have proved the superiority of combined conventional CT and high resolution CT over chest radiograph in the detection of silicotic lesions such as nodules, mild emphysematous change, septal thickening of secondary lobules and so on,[3,5,7] but the relationship between CT findings and lung function is still unclear. Collins et al.[8] have reported that they were unable to correlate the presence of nodules in HRCT with any abnormality in air-flow, lung volume or resting gas exchange. Bergin et al.[7] reported that the reduced levels of lung function in patients with silicosis correlated with superimposed emphysema rather than nodular profusion. Meanwhile, one study[9] has established a relationship between disease severity and the loss of lung function in silicosis. These different results could be due to differences in research methods. One more important factor is that pulmonary function examination is an effort-dependent method, and furthermore, it provides integrated overall values in which subtle regional changes are elusive.

In this study we tried to use technegas to assess the ventilation status of patients with silicosis and compare it with the morphologic changes shown by CT. As Burch et al.[11] reported, technegas has considerably small particle size and can reach the peripheral parts of the lungs. Several researches reported that technegas gives similar or better diagnostic information on lung ventilation imaging in qualitative comparison with xenon-133[14–16] and krypton-81m.[17–19] Another characteristic of technegas is that its particles are hydrophobic and dissolve in organic solution only.[20] This means that technegas particles do not induce condensation of water in the humid atmosphere of the lung due to their hydrophobic nature, leading to a stable size distribution. On the other hand, the pathological characteristic of silicosis is diffused fibrosis. CT-pathologic correlation studies have shown that nodules corresponded to whirled, hyalinized fibrosis around the respiratory bronchioles and septal thickening due to irregular fibrosis or edema.[21,22] Other pathological changes, such as emphysema and bulla formation, will also be involved in this pathological process. These pathological changes result mainly in obstructive pulmonary impairment. It is therefore considered that when technegas is inhaled, its distribution may be influenced by this pathological process. Our results showed that the distribution of technegas became heterogeneous with the degree of severity of silicosis on SPECT images.

Small diffuse lesions, as in silicosis, are difficult to detect as cold spots of radioactivity, because the size of these kinds of lesions is under the FWHM of SPECT. To measure such small lesions in a quantitative way, we considered describing these small scattered pathological processes as the inhomogeneous fluctuated distribution of technegas on SPECT. In order to eliminate the dispersion due to counting statics from that of inhomogeneity, we used a coefficient of variation (CV) which was obtained by dividing the variance in the counting activity of each ROI by the mean pixel count for the zone.

But care must be taken in applying this analytical approach to see that the CV value is also related with the type of filter that is used in the process of reconstruction of the SPECT images. That is, according to the phantom study, if the high frequency band was cut too much it would result in smoothing the existence of inhomogeneity originating in the scattered subliminal defects and if cut less it would result in a noisy image with an unduly high CV values. A 0.15 Butterworth filter was determined to be adequate according to the phantom studies described.

We sampled the peripheral parts of the lung and avoided touching the contours of the lung, because the real contour of the lung can not be exactly known in the SPECT image. The position of the ROI in the SPECT image corresponded exactly to the CT image. Our results showed that the morphologic changes in the CT image correlated to functional changes in the SPECT image well. Our results also showed that the CV value was significantly greater in patients than in controls. An attempt was made to correlate the extent of each CT abnormality with the CV value. We observed a marked, although low, correlation between the extent score for CT abnormalities and the CV value. The CV value may be mainly determined by the profusion of nodules, bulla and septal thickening.

In conclusion, this study has shown that the abnormal CT findings of silicosis were well correlated to the regional ventilation impairment seen on SPECT. The CV value was significantly higher in silicosis than without silicosis. The CV value was mainly determined by the extent of the profusion of nodules, bulla and septal thickening. It is considered that the CV value can express the functional state of the silicotic lung.

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