RESPIRATORY INFECTION

Six month radiological and physiological outcomes in severe acute respiratory syndrome (SARS) survivors

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Thorax 2004;**59**:889–891. doi: 10.1136/thx.2004.023762

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Received 23 February 2004
Accepted 10 May 2004

Background: The long term physiological and radiological outcomes of SARS survivors and their possible determinants are uncertain.
Methods: SARS survivors in a follow up clinic in a regional hospital underwent high resolution computed tomography (HRCT) of the thorax and lung function tests 6 months after admission to hospital. The associations between the clinical and demographic data of the patients and the physiological and radiological outcomes were examined.
Results: Fifty seven patients took part in the study. Lung function abnormalities were detected in 43 patients (75.4%), with restrictive defects (n = 16) being most common (28.1%). Radiological abnormalities of any degree were detected in 43 patients (75.4%). Only the use of pulse corticosteroids was associated with the presence of CT abnormalities (p = 0.043, OR 6.65, 95% CI 1.06 to 41.73).
Conclusions: Physiological and radiological abnormalities are still present in a considerable proportion of SARS survivors at 6 months.

Severe adult respiratory syndrome (SARS) is associated with considerable mortality and morbidity.[1] A significant proportion of these patients require intensive care and mechanical ventilation. Residual deficits in the structural and physiological functions of the respiratory system might occur in patients with such severe pneumonias. Although there have been reports on short term radiological outcomes,[2–5] the long term outcome of SARS survivors has not been reported. We present the results of lung function tests and high resolution computed tomography (HRCT) of the thorax in these patients 6 months after their initial hospital admission with SARS.

METHODS

Patients

All 93 adult patients who had the SARS outbreak were evaluated regularly in the Post-SARS Clinic at the Queen Elizabeth Hospital, a regional hospital in Hong Kong. Six months after admission to hospital arrangements were made for them to undergo lung function tests and HRCT scanning of the thorax. All patients enrolled had positive laboratory evidence of SARS infection with either positive reverse transcriptase polymerase chain reaction (RT-PCR) to SARS related coronavirus (SARS-CoV) from clinical specimens or positive SARS-CoV IgG antibody seroconversion during the convalescence phase.

The study was approved by the ethics committee of Queen Elizabeth Hospital and written informed consent was obtained from all patients.

Pulmonary function testing

Pulmonary function tests were conducted in the Lung Function Laboratory of Queen Elizabeth Hospital using the SensorMedics Autobox Plethysmograph (Sensormedics Inc, Yorba Linda, CA, USA) according to American Thoracic Society (ATS) guidelines.[6] Lung volumes were determined by the nitrogen washout method and the transfer factor was determined by the single breath carbon monoxide method.

HRCT scanning

A multidetector CT scanner (Sensation 16; Siemens) was employed using the non-contrast technique with the following parameters: 0.75 mm detector collimation; 13.5 mm feed/rotation; 0.5 s/rotation; 120 kV, and 120 effective mA. The reconstructed 1 mm thick images were studied in a viewing console. The radiological extents were scored independently by two radiologists who were blind to the clinical data and final scores were established by consensus. The scoring system was based on reports of radiological progress of SARS and was dependent on the number of lung segments involved (maximum 18).[2–4 7] The severity was classified into four grades (grade 0: no involvement; grade 1: $\leqslant$50% of the lung segment involved by residual ground glass opacification with/without reticulation; grade 2: >50% lung segments involved by ground glass opacification with/without interstitial thickening; grade 3: evidence of lung fibrosis such as thick parenchymal bands, architectural distortion, traction bronchiectasis). In the statistical analysis, individual segmental scores were added together to give a summation score (maximum 54 points).

Statistical analysis

Lung function results were expressed as percentage predicted of established reference values. The number and severity of lung segments involved were expressed as median values with interquartile ranges (IQR). Non-parametric data were analysed using the Mann-Whitney test with a significance level set at 0.05. Univariate analysis was performed to compare the characteristics of patients with normal and abnormal HRCT scans using the independent Student's *t* test for continuous variables and Pearson χ^2 or Fisher exact test for categorical variables. Logistic regression analysis was used to study the independent covariates for the presence of HRCT abnormalities. Statistical analyses were performed using SPSS Version 11.0.

RESULTS

Fifty seven of the 93 adult survivors completed the study (seven defaulted during the follow up period, 13 had no seroconversion, five refused, and 11 either failed to perform lung function studies or missed the HRCT appointments at the close of study). Their mean (SD) age was 38.1 (10.7) and 38.6% were men. Six patients (10.6%) had underlying co-morbidities (diabetes mellitus 7%, hypertension 1.8%,

Table 1 Univariate analysis of predictors of abnormal CT scores

	Normal CT score (n = 14)	Abnormal CT score (n = 43)	p value
Mean (SD) age (years)	34.6 (7.6)	39.3 (11.4)	0.163
Sex (% female)	42.9%	67.4%	0.101
Current smoker (%)	14.3%	2.33%	0.146
Neutrophil count on admission (10^9/l)	4.05 (1.83)	4.21 (1.96)	0.793
Lymphocyte count on admission (10^9/l)	0.91 (0.28)	0.74 (3.12)	0.089
Lactate dehydrogenase on admission (IU/l)	517.4 (180.9)	539.5 (332.2)	0.814
Abnormal FEV_1 (<80% predicted normal)	14.3%	16.3%	0.859
Abnormal $FEF_{25-75\%}$ (<80% predicted normal)	21.4%	44.1%	0.129
Abnormal FVC (<80% predicted normal)	7.14%	6.98%	0.983
Abnormal TLCO (<80% predicted normal)	71.4%	62.8%	0.556
Abnormal TLC (<80% predicted normal)	28.6%	30.2%	0.906
Median (IQR) CXR peak score	5.5 (3.75–11.25)	12 (7.0–18.0)	0.022
Pulse steroid use (yes)	57.1%	93.0%	0.004
History of ICU admission (yes)	21.4%	32.6%	0.429
History of intubation (yes)	14.3%	23.3%	0.475

FEV_1, forced expiratory volume in 1 second; FVC, forced vital capacity; TLCO, carbon monoxide transfer factor; TLC, total lung capacity; CXR, chest radiograph; ICU, intensive care unit.

cardiovascular diseases 1.8%); no underlying pulmonary diseases were observed. Only three patients were smokers. Pulse corticosteroids were used in 48 patients (84.2%); 17 (29.8%) required intensive care and 12 (21.1%) required mechanical ventilation. There was no statistically significant difference between the study group and those who were excluded in terms of mean age ($p = 0.3$), male sex ($p = 0.89$), pulse corticosteroid use ($p = 0.141$), intensive care admission ($p = 0.655$), and mechanical ventilation ($p = 0.605$).

Even though symptoms were not systematically recorded, most (if not all) patients were free of respiratory symptoms at follow up. Lung function abnormalities were detected in 43 patients (75.4%): mild obstructive defect in one (1.8%), mild restrictive defect in 14 (24.6%), moderate restrictive defect in two (3.5 %), and mixed defects in two (3.5%). Isolated reductions in the carbon monoxide transfer factor (TLCO) were found in 20 patients (median 63% predicted, IQR 56.5–73.5). Seventeen had abnormal total lung capacity (TLC) (median 68.5% predicted, IQR 68.5–75.0) and four patients had abnormal functional vital capacity (FVC) (median 69.5% predicted, IQR 63.3–75.8) No significant differences were identified between patients with normal and abnormal lung function.

Radiological abnormalities of any degree were detected in 43 patients (75.4%). The median number of segments involved was 3 (IQR 0.5–9.5) and the median total score was 3 (IQR 0.5–11.0). In the majority of patients (28.1%) 1–3 segments were involved. The lower lobes were involved in 41 patients (71.9%) while the upper lobes were involved in 31 (54.4%; $p<0.006$). The severity of residual radiological abnormalities, measured as median HRCT score per unit segment involved, was 0.2 (IQR 0–0.5) in the upper lobes and 0.2 (IQR 0–0.8) in the lower lobes with no significant differences observed ($p = 0.34$). Eight patients (14%) had the worst score of 3 in one of their lung segments. Only the use of pulse steroids was found to be an independent factor associated with the presence of CT abnormalities ($p = 0.043$, OR 6.65, 95% CI 1.06 to 41.73; tables 1 and 2).

Table 2 Multivariate analysis of predictors of abnormal CT score

	Odds ratio	p value	95% CI
Age	1.02	0.62	0.95 to 1.10
Lymphocyte count (10^9/l)	1.00	0.84	0.99 to 1.01
CXR peak score	1.04	0.55	0.92 to 1.18
Pulse steroid	6.65	0.043	1.06 to 41.73

CXR, chest radiograph.

DISCUSSION

Few reports have described the outcome of SARS survivors,[2–5] and ours is the first to report the long term effects on changes in both pulmonary function and HRCT imaging. At 6 months, residual abnormalities of pulmonary function were still observed in three quarters of the cohort, mostly consisting of isolated reductions in TLCO with a small number of restrictive defects. This is higher than those reported in other cohorts.[5] There are few data on the physiological outcome of patients with pneumonia, although in ARDS survivors physiological abnormalities have been reported at 6 months.[8 9] Isolated abnormalities in TLCO could represent pulmonary fibrosis or a late phase in the course of recovery, being identified in a longitudinal study.[9] Cardiopulmonary exercise testing might further reveal reduced pulmonary gas exchange in patients with normal TLCO.[8] The rate of radiological abnormalities (75%) is lower than that reported in an earlier study (96%) 1 month after admission,[2] which suggests that radiological abnormalities caused by SARS might improve over time. A similar rate of residual radiographic changes was also identified in ARDS survivors.[10] However, ARDS may not be analogous with SARS as it only occurred in a subset of SARS patients. The association between the use of pulse corticosteroids and radiographic changes may not be causal as the former might just reflect more severe disease and hence more residual lung damage.

Our study is limited by the small sample size and might therefore incur a type II error. Since this is a cross sectional analytical study, longitudinal data on the progress of observed physiological and radiological abnormalities have not been addressed. Future studies of the association between objective measurements of functional status (such as the exercise lung function test or 6 minute walk test) and the physiological and radiological defects may produce more interesting findings.

In conclusion, we have shown that significant radiographic and physiological abnormalities still exist in a high proportion of SARS patients 6 months after disease onset. It is important to follow up survivors of this disease to reveal any long term effects.

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