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Long-term sequelae of SARS: physical, neuropsychiatric, and quality-of-life assessment

Key Messages

1. Impairment of lung diffusing capacity persisted in 24% of SARS survivors; their exercise capacity and health status were markedly lower than the general population at 1 year after illness onset.
2. There was no difference in lung function indices, exercise capacity, and health status at 1 year between the intubated and non-intubated SARS patients admitted to the intensive care unit, although the former had more severe lung injury.
3. The functional disability in SARS survivors appears out of proportion to the degree of lung function impairment and may be due to additional factors such as muscle deconditioning, steroid-related musculoskeletal complications, critical illness-related neuropathy/myopathy, and/or psychological factors.

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Introduction

The emergence of SARS in Southern China in November 2002, followed by the global outbreak in 2003, caught the medical profession by surprise.[1] Studies on SARS-coronavirus viral loads have shown that peak viral levels were reached at the second week of illness when patients were in hospital care, and thus health care workers (HCWs) were particularly prone to infection.[2,3] About 20 to 36% of SARS patients were admitted to the intensive care unit (ICU), whereas 13 to 26% progressed to acute respiratory distress syndrome (ARDS) and received invasive ventilatory support.[2,4,5]

In our hospital, over half of those infected were HCWs.[4] At 5 weeks after discharge, high-resolution computed tomography for 24 out-patients with residual radiological opacities revealed multiple patchy ground glass appearance and interstitial thickening (n=9, 38%) and fibrotic changes (n=15, 62%).[6] Serial lung function, exercise capacity, chest radiographs, and health-related quality of life (HRQoL) were examined at 3, 6, and 12 months after illness onset, and SARS survivors who had been admitted to the ICU were compared to those who were only treated in medical wards.[7,8]

Aims and objectives

To examine the impact of SARS on pulmonary function, exercise capacity, and HRQoL among survivors.

Methods

This was a prospective longitudinal follow-up study of patients with SARS discharged from our hospital after surviving the outbreak in 2003. The patients came from our previously reported cohort[4] recruited over a period of 2 weeks from 11 to 25 March 2003. All patients in this study had laboratory-confirmed SARS.[9]

Following discharge, lung functions of patients were evaluated at the end of 3, 6 and 12 months after disease onset. Subjects were interviewed and underwent physical examination, pulmonary function testing, respiratory muscle strength measurement, posteroanterior chest radiography, resting oximetry, and a standardised 6-minute-walk (6MW) test. In addition, they completed the Medical Outcomes Study 36-item Short-Form General Health Survey (SF 36) to measure HRQoL. The 6MW distances obtained for each patient on 2 separate days were compared to the normative reference data collected from a population survey of 538 normal healthy subjects in 2004 by the Coordinating Committee in Physiotherapy of the Hong Kong Hospital Authority.[7,8]

Lung volumes (total lung capacity [TLC], vital capacity [VC], residual volume [RV], functional residual capacity [FRC] using the nitrogen washout method), spirometry (forced vital capacity [FVC], forced expiratory volume in one second [FEV_1], FEV_1/FVC ratio, forced expiratory flow rate over middle 50% of FVC [FEF_{25-75}]), and surface area for gas exchange (diffusion capacity adjusted for haemoglobin [DLCO] and DLCO per alveolar volume [K_{CO}]) were

performed with the Vmax System (SensorMedics Corp, CA, USA). The DLCO was determined by the single-breath carbon monoxide technique using an infrared analyser. The results were compared to available normative data[10] widely adopted as reference values in Hong Kong before 2006.

Results

Of the first 138 patients infected with SARS in March 2003, 15 (11%) died.[4,9] Among the 123 survivors, 13 (11%) did not attend for follow-up at 3 and 6 months,[7] whereas another 13 (11%) defaulted the 12-month assessment.[8] Thus, 44 males and 66 females with a mean age of 36 (standard deviation [SD], 10) years and body mass index of 23 (SD, 5) kg/m^2 completed the 6-month assessment. Seventy (64%) of them were HCWs.

At 6 months, 33 (30%) of the subjects had abnormal chest radiographs. Four (4%), 8 (7%), and 17 (16%) patients had FVC, TLC, and DLCO values below 80% of predicted, respectively; whereas 15 (14%) and 24 (22%) had Pimax and Pemax values below 80 cm H_2O, respectively. The mean 6MW distance increased from 464 (SD, 83) m at 3 months to 502 (SD, 95) m (95% confidence interval [CI], 22-54 m, P<0.001), but this distance was shorter than in normal controls in the same age-groups, indicating impairment of HRQoL at 6 months.[7]

At 1 year, 39 males and 58 females completed the serial assessments; 63 (70%) of them were HCWs with a mean age of 40 (SD, 10) years and mean body mass index of 24 (SD, 4) kg/m^2. Twenty-seven (28%) of the patients had abnormal chest radiographs. Four (4%), 5 (5%), and 23 (24%) of the patients had FVC, TLC, and DLCO values below 80% of predicted, respectively. The mean 6MW distance was 511 (SD, 90) m, which was higher than that at 3 months (mean difference, 47; 95% CI, 32-62 m; P<0.01) but not different from that at 6 months (mean difference, 10; 95% CI, -4 to 24 m, P=0.18). The 6MW distance of the survivors was less than that in normal controls of the same age-groups, indicating impairment of HRQoL at 12 months. Patients admitted to the ICU (n=31) had higher mean chest radiograph scores (1.6 [SD, 3.1] vs 0.4 [SD, 1.1], P=0.04) and lower % predicted FVC, TLC, and DLCO values than those not admitted to the ICU, but there were no significant differences with respect to their 6MW distance and health status.[8]

Discussion

This prospective cohort study has shown that 24% and 28% of SARS survivors had impaired lung diffusing capacity and abnormal chest radiographs, respectively, at 1 year after illness onset. Overall, the serial assessments of 6MW distance revealed significant improvement over 12 months, though exercise capacity and health status were still significantly lower than in normal controls of the same age-groups. The 1-year lung function indices in SARS survivors who were admitted to ICU were markedly inferior to those who were only treated on medical wards, although no significant differences were noted for the 6MW distances, respiratory muscle strength, and health status between the two groups. Interestingly, there was no difference in lung function indices, exercise capacity, and health status at 1 year between intubated and non-intubated ICU SARS patients, although the former had more severe lung injury.[8]

Despite the presence of extensive parenchymal changes on computed tomography during the early convalescent period,[6] surprisingly most lung function test indices of SARS patients were within normal limits in most of our patients.[7,8] Their poor exercise performance appeared out of proportion to the degree of lung function impairment and may be due to extra-pulmonary factors such as muscle deconditioning, steroid or viral-induced myopathy, critical illness polyneuropathy/myopathy,[11] and/or other psychological factors. Eighteen out of 44 SARS survivors in Singapore had reduced exercise capacity at 3 months after discharge, which could not be accounted for by impairment of pulmonary function.[12] The inability to exercise in their recovered SARS patients was primarily due to extra-pulmonary causes such as physical deconditioning and steroid myopathy. Among our SARS survivors, at 3 months after illness onset, strength and endurance were more impaired in proximal than distal muscles.[13]

Among SARS survivors, persistent lung function abnormalities occurred in less than one third of patients at 1 year, and yet there was a significant impairment of health status.[8,14-16] The results are not surprising, as these patients endured long periods of isolation and extreme uncertainty during the SARS illness that could have created enormous psychological stress[17] and mood disturbances,[18] in addition to the physical impairment. In addition, steroid toxicity, personal vulnerability, and psychosocial stressors might have jointly contributed to the development of psychosis in some patients.[19] Longer term follow-up is needed to assess whether these effects persist.

Conclusions

Significant impairment of diffusing capacity persisted in 24% of SARS survivors; at 12 months after illness onset their exercise capacity and health status were markedly diminished compared to the general population. Further follow-up is needed to assess if these deficits persist.

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1. Hui DS, Joynt GM, Wong KT, et al. Impact of severe acute respiratory syndrome (SARS) on pulmonary function, functional capacity and quality of life in a

cohort of survivors. Thorax 2005;60:401-9.

2. Hui DS, Wong KT, Ko FW, et al. The 1-year impact of severe acute respiratory syndrome on pulmonary function, exercise capacity, and quality of life in a cohort of survivors. Chest 2005;128:2247-61.

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