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Correlation of clinical outcomes and radiographic features in SARS patients

Key Message

In SARS patients, more extensive airspace disease on chest radiographs at presentation is an independent predictor of adverse outcome (admission to the intensive care unit or death).

Introduction

In March 2003, there was a major outbreak of SARS in Hong Kong. In the Prince of Wales Hospital, 138 patients including health care workers contracted the disease. Of these patients, 23% progressed to acute respiratory failure for which they were admitted to the intensive care unit (ICU), whereas 14% of the 138 patients received invasive mechanical support within 1 to 2 weeks.[1] Chest radiography remains the first-line radiological investigation in suspected cases and helps monitor progress during treatment. Air-space opacity in peripheral and lower-zone distribution was most commonly seen at presentation. It then progressed to multi-focal or bilateral lung involvement; about 70% of SARS patients showed improvement.[2]

Severity of lung abnormalities on chest radiographs correlates positively with clinical and laboratory parameters, such as SaO_2 and liver enzymes, including alanine aminotransferase (ALT) and aspartate aminotransferase (AST) levels.[3] Moreover, there are correlations between radiographic parameters, oxygen supplementation, and apparent response to treatment.[4] We aimed to evaluate the correlation between clinical outcome and the radiographic features of SARS patients.

Methods

Patients

A cohort admitted from 11 to 25 March 2003 were analysed.[1] There were 66 males and 72 females with a mean age of 39 (standard deviation [SD], 17) years. All patients were ethnic Chinese. Clinical and laboratory data were recorded up to 5 April 2003.

Diagnosis and monitoring of progress

The diagnosis of SARS was based on the Centers for Disease Control criteria.[5] Initial investigations included complete blood count, clotting profile (prothrombin time [PT], activated partial thromboplastin time [APTT], international normalised ratio [INR], D-dimer) and serum biochemistry (including electrolytes, renal function test, liver function test, creatinine kinase [CPK], lactate dehydrogenase [LDH]). The INR was measured because some patients might develop disseminated intravascular coagulation. These parameters and chest radiographs were monitored daily. Resort to supplemental oxygen and timing of pulse methylprednisolone during the study period were also recorded.

Treatment

Patients who developed hypoxia were given oxygen therapy through nasal cannulae. Patients were admitted to the ICU when they developed respiratory failure as evidenced by: (1) failure to maintain an arterial oxygen saturation of at least 90% while receiving supplemental oxygen of 50%, and/or (2) a respiratory rate greater than 35 breaths per minute. Nineteen (14%) patients received invasive mechanical ventilation.

Radiographic assessment

Anteroposterior chest radiographs of the 138 patients were taken at presentation

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and daily during the hospital stay. All 2045 radiographs were assessed (a mean of 15 per patient; range, 3-26) by three radiologists (who were unaware of the clinical progress) and consensus reached. Each lung was divided into three zones (upper, middle and lower). Each zone spanned one third of the craniocaudal distance of the lung and was evaluated separately. The presence, appearance, distribution and size of lung parenchymal abnormalities on each radiograph were recorded. The area (%) of lung involved in each zone was estimated visually; the maximum % of each zone was 100%. The overall mean % of lung parenchymal involvement of the six lung zones could range from 0% to 100%.[2]

The progression pattern based on serial chest radiographs was categorised into four patterns according to our previous study.[2] Type 1 referred to: initial deterioration to peak level followed by improvement, peak level defined as overall mean lung involvement of >25% of the initial extent. Type 2 referred to: fluctuating radiographic changes, with at least two peaks and an intervening trough, trough level defined as overall mean lung involvement differing from the peak level by >25%. Type 3 referred to: static radiographic changes, with no apparent peak (ie change in overall mean lung involvement <25% of the initial extent) for more than 10 days. Type 4 referred to: progressive radiographic deterioration with no improvement.

Table 1. The extent of consolidation on initial chest radiographs of 138 SARS patients

Extent of consolidation (%)	No. (%) of patients
0	30 (22)
0.1-2.5	58 (42)
2.6-5.0	29 (21)
5.1-10	10 (7)
10.1-15	6 (4)
>15	5 (4)

Table 2. The number of lung zones involved on initial chest radiographs of 138 SARS patients

No. of lung zones involved*	No. of patients	Median (interquartile range) interval of chest radiographs taken after fever onset (days)
0	30	1.5 (0-5)
1	59	2.0 (0-9)
2	28	2.0 (0-10)
3	12	3.5 (0-10)
4	6	2.5 (0-6)
5	1	3.0 (3-3)
6	2	3.5 (0-7)

* Each lung is divided into three zones: upper, middle, and lower. Each zone spans one third of the craniocaudal distance of the lung on an anteroposterior chest radiograph

Results

Findings on chest radiograph

On average the initial chest radiograph was taken 2.5 days after the onset of fever (range, 0-10 days). A total of 108 of the 138 (78%) patients had air-space opacity at presentation; 59 (55%) had focal unilateral opacities and 49 (45%) had unilateral multi-focal or bilateral involvement. Initial radiographs of 30 (22%) patients were normal, but 29 of them had air-space opacities on follow-up radiographs 1 to 7 days (median, 3 days) later.[2] At presentation, the overall mean lung involvement was 5% (range, 1-63%).[2] The extent of consolidation and number of zones involved on the initial radiographs are summarised in Tables 1 and 2, respectively.[6] Regarding the pattern of progression, type 1 was the most common (97/138, 70%), followed by type 2 (24/138, 17%), type 3 (10/138, 7%), and type 4 (7/138, 5%).[2]

The peak of the extent of pneumonic changes corresponded to the time of commencement of pulse intravenous methylprednisolone treatment. Consolidation peaked at a mean interval of 9 (SD, 3) days after fever onset. The median time of starting the first pulse of methylprednisolone was 8 days after fever onset (interquartile range [IQR], 6-9 days).

Laboratory results

The initial blood counts showed leukopaenia (total white cell count of <3.5 x10^9/L; normal range [NR], 3.5-10.5 x10^9/L) in 47 (34%) of the patients. The neutrophil count was within normal limits in most cases (median, 3.5 x10^9/L; range, 0.5-11.8 x10^9/L; NR, 1.5-6.6 x10^9/L), but a moderate lymphopaenia (absolute lymphocyte of <1.0 x10^9/L; NR, 1.0-3.5 x10^9/L) was present in 96 (70%) of the patients.[1] Biochemistry measurements revealed elevated serum ALT in 32 (23%) of the patients (mean, 60.4; SD, 150.4; NR, <55 IU/mL); CPK was elevated in 44 (32%) of the patients (median, 126; range, 29-4644; NR, 42-218 U/L), whereas the LDH was elevated in 98 (71%) of the patients. At presentation, the mean LDH was 287.7 (SD, 143.3; NR, 87-213) U/L for those not admitted to the ICU and 558 (SD, 258) U/L for those admitted to the ICU or dead (P<0.001). The mean peak LDH was 310 (SD, 153.8) U/L for the former and 629.7 (SD, 283.5) U/L for the latter (P<0.001).[1]

Clinical outcomes

Of the 138 patients, 36 (26%) were admitted to the ICU due to respiratory failure. In the first 4 weeks of the outbreak, there were eight deaths (crude mortality rate=6%) related to severe respiratory failure: six died in the ICU and two on medical wards; all were originally admitted for other major medical conditions. In total, 38 patients reached the clinical end-point for poor outcome (ie ICU admission or death).

Correlation between clinical outcome and radiographic features

Compared to survivors not admitted to ICU, those admitted

Table 3. Correlation between clinical outcomes and radiographic features*

Radiographic feature	Patients who received ICU care and/or died	Surviving patients who did not receive ICU care
Median (interquartile range) extent of consolidation (%)		
Day 0	3.3 (1.7-8.8)	1.7 (0.0-3.3)
Day 7	15.0 (6.5-28.7)	5.0 (2.5-7.5)
No. of lung zones involved		
Day 0		
≤1 (n=89)	14 (16)	75 (84)
>1 (n=49)	24 (49)	25 (51)
Day 1		
≤1 (n=56)	3 (5)	53 (95)
>1 (n=82)	35 (43)	47 (57)
Consolidation at day 0		
Unilateral (n=67)	13 (19)	54 (81)
Bilateral (n=41)	22 (54)	19 (46)
Progression pattern		
Type 1 (n=97)	17 (18)	80 (83)
Types 2-4 (n=41)	21 (51)	20 (49)

* Unless otherwise stated, data are presented as no. (%) of patients

to ICU or died had more extensive radiographic evidence of pneumonia on the initial-day (median, 1.7% vs 3.3%; IQR, 0-3.3% vs 1.7-8.8%; P<0.001) and day-7 (after fever onset) radiographs (median, 5% vs 15%; IQR, 2.5-7.5% vs 6.5-28.7%; P<0.001, Table 3).

Compared to those with one or less than one zone involved, those with more than one zone involved on the initial day (14/89 vs 24/49, P<0.001) and day 7 (3/56 vs 35/82, P<0.001) were significantly more likely to have been admitted to the ICU or dead (Table 3).

Patients with bilateral pneumonic changes on the initial radiograph were more likely to have been admitted to the ICU or dead than those with unilateral involvement (22/41 vs 13/67, P<0.001, Table 3).

Among the 97 patients with type-1 radiographic pattern, only 17 (18%) were admitted to the ICU or dead, as opposed to 21 (51%) of the 41 patients with types 2 to 4 patterns (P<0.001). Of these 21 patients, 14 had type-2 and seven type-4 patterns (Table 3).

The cumulative % of patients with SARS not receiving supplementary oxygen versus the extent of consolidation is shown in the Kaplan-Meier curve in the Figure.[6]

The rate of change of LDH (units/day) correlated with the rate of change of % involvement in chest radiographs (Spearman r_s=0.40, P=0.014).

Univariate analysis revealed that advanced age, male gender, peak CPK value, LDH at presentation and its peak value, higher initial absolute neutrophil counts, and low serum sodium levels were predictive factors for ICU admission and death.[1] Following multivariable analysis, other independent predictors of adverse outcomes were identified.[6] These included: the number of zones involved in initial chest radiographs, advanced age (odds ratio [OR] per year=1.1; 95% CI=1.0-1.1; P<0.001), high baseline LDH (OR per U/L=1.0; 95% CI=1.0-1.0; P=0.001), higher absolute neutrophil counts at presentation (OR=1.4; 95% CI=1.0-1.8; P=0.025), and more than one zone involved in initial chest radiographs (OR=3.2; 95% CI=1.1-9.3; P=0.037).

Discussion

SARS was a new infectious disease with a high morbidity and mortality. It usually progressed to acute respiratory failure within a week, with radiographic evidence of air-space disease. Chest radiography (supplemented by thin-section computed tomography of the thorax in selected cases) is a useful diagnostic and management tool. At presentation, 78% of our patients had evidence of air space consolidation on their chest radiographs. Initial radiographs were normal in over 20% of patients, but follow-up radiographs showed abnormality at a median of 3 days.[2]

In some patients, consolidation may progress to respiratory failure, ICU admission, and/or death. Progression of consolidation peaked at a mean of 9 (SD, 3) days from fever onset. There appeared to be a strong correlation between the extent of radiographic abnormality and the degree of respiratory failure. This can be inferred from the Kaplan-Meier plot (Fig). Even if only a small percentage (10%) of the lung showed consolidation, approximately 50% of such patients received supplementary oxygen. Based on evidence of progression on serial chest radiographs, intravenous pulse methylprednisolone was administered in order to control immune-mediated lung injury; the median time of commencement was 8 days from the onset of symptoms. Although a favourable clinical response appeared to have been achieved in most patients, 36 (26%) received ICU care and eight died.

In view of the high proportion of SARS patients receiving ICU care, it would have been desirable to have parameters that help predict clinical outcome. In that respect, the radiographic extent of pneumonia at presentation appeared to correlate with adverse clinical outcomes. More extensive air-space diseases (as reflected by a higher % of consolidation, more than one zone being involved in chest radiographs on admission and on day 7 after fever onset, and bilateral disease) were associated with subsequent ICU admission or death. This finding is similar to other forms of community-acquired pneumonia in general, including the ICU-treated populations with abnormal air-space opacities in both lungs, more than one lobe involved, and rapid radiographic progression, all of which

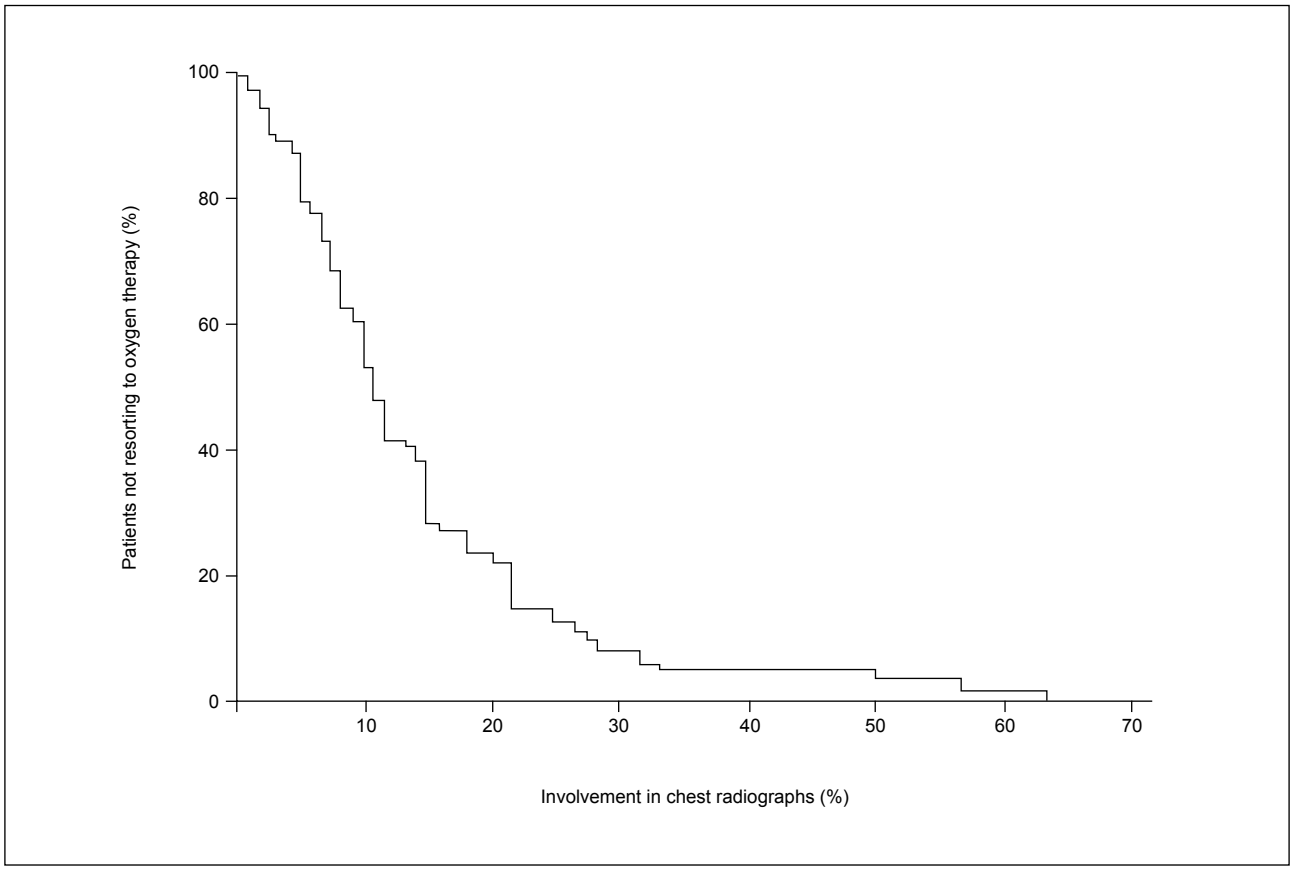

Fig. Kaplan-Meier curve of cumulative % of patients with SARS free of supplementary oxygen requirement versus the extent of consolidation
Even if only a small percentage (10%) of the lung showed consolidation, approximately 50% of such patients received supplementary oxygen[6]

were independent predictors of poor outcome. The radiographic pattern of progression also correlated with clinical outcome. Patients with type-1 pattern seemed to have more favourable outcomes. By contrast, all seven patients with type-4 pattern (progressive deterioration) had adverse clinical outcomes; six died and the seventh was critically ill and had a prolonged ICU stay.[6] Chest radiographs correlate positively with the rate of change of LDH, a marker of tissue damage. The LDH can reflect the extent of lung injury, and both serial chest radiographs and LDH levels are important in the management of SARS. After multivariable analysis, more than one zone being involved in initial chest radiographs was an independent predictor of adverse outcomes even after adjusting for high baseline LDH levels, advanced age, and high neutrophil counts.[6]

Conclusions

In SARS patients, more extensive airspace disease at presentation is an independent predictor of adverse outcome (ICU admission or death).[6] Chest radiography is therefore a useful diagnostic and management tool.

Acknowledgements

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Hui DS, Wong KT, Antonio GE, et al. Severe acute respiratory syndrome: correlation between clinical outcome and radiologic features. Radiology 2004;233:579-85.

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