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American Journal of Emergency Medicine (2005) **23**, 525–530

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The American Journal of Emergency Medicine

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Chest radiograph screening for severe acute respiratory syndrome in the ED

Stewart Siu-Wa Chan MBBS(Syd), FRCSEd, FHKAM[a,*]
Paulina Siu-Kuen Mak BN[a], Kwok Kuen Shing MBChB, FRCR[b],
Po Nin Chan MBChB, FRCR[b], Wing Hung Ng MBChB, FRCR[b],
Timothy Hudson Rainer MD, BSc, MBBCh, MRCP, FHKAM[a]

[a]*Accident and Emergency Medicine Academic Unit, Prince of Wales Hospital, The Chinese, University of Hong Kong, Shatin, Hong Kong*
[b]*Department of Diagnostic Radiology and Organ Imaging, Prince of Wales Hospital, The Chinese, University of Hong Kong, Shatin, Hong Kong*

Received 21 July 2004; accepted 18 October 2004

Abstract The purpose of the study was to evaluate the use of chest radiography for the screening of severe acute respiratory syndrome (SARS). We retrospectively analyzed all patients who attended an Emergency Department SARS screening clinic during the outbreak in Hong Kong, from March 10 to June 5, 2003. Patients with clinical and epidemiologic suspicion of SARS were evaluated by serial chest radiography. All radiographs were reported by consensus from 2 radiologists, blinded to the clinical records. The prevalence of SARS was 13.3% among 1328 patients included. The initial radiograph had sensitivity 50.3%, specificity 95.0%, positive likelihood ratio 10.06, negative likelihood ratio 0.52, positive predictive value 61.5%, and negative predictive value 92.3% for diagnosing SARS. Serial chest radiography had sensitivity 94.4%, specificity 93.9%, positive likelihood ratio 15.48, negative likelihood ratio 0.06, positive predictive value 71.4%, and negative predictive value 99.0%. The initial chest radiograph has poor sensitivity, and serial radiographs are required to rule out SARS.

1. Introduction

The resurgence of severe acute respiratory syndrome (SARS) has been a topic of much interest. During April 22 to 29, 2004, the Chinese Ministry of Health reported a total of 9 new cases of SARS in China; 7 of the patients were from Beijing and 2 were from Anhui Province, located in east-central China. In January 2004, 4 confirmed cases were reported in Guangdong Province, southern China. The likely reemergence of this disease in Hong Kong has pressurized frontline health care workers, especially those working in EDs. The ED has to assume the challenging role of administering a rapid and accurate screen for SARS, at the same time of carrying out appropriate containment and infection control measures. Because of the high infectivity and high mortality nature of SARS, prompt diagnosis is

* Corresponding author. Tel.: +852 2632 2219; fax: +852 2337 3226.
E-mail address: saukau@netvigator.com (S.S.-W. Chan).

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doi:10.1016/j.ajem.2004.10.014

essential. However, early clinical features of SARS are often nonspecific, and investigations have shown that screening at the ED is aided by laboratory and radiographic investigations [1-6]. Various symptom scores and associated prediction rules, applicable to the ED setting, have recently been derived and validated, and reported in emergency medicine literature [2,4,5]. This study mainly focuses on the use of chest radiography as a screening tool.

It is recognized that chest radiography plays an important role in the diagnosis of SARS [1,3,4,7-22]. At fever onset, almost 80% of patients with SARS had abnormal chest radiographs [9]. However, the sensitivity and specificity of chest radiography before fever onset and at early stages of the disease is not known. Chest radiographic abnormality may precede lower respiratory tract symptoms in some patients with SARS [3,22]. For suspicious cases of SARS with initially normal chest films, repeating chest radiography every 1 to 3 days is likely to increase the yield [20]. However, as yet, this subject has also not seen investigated in detail.

During the outbreak of SARS in Hong Kong that started in March 2003, the ED of Prince of Wales Hospital operated a screening center to evaluate patients with epidemiologic and clinical suspicion of SARS. The authors retrospectively analyzed all cases that were screened at the ED and followed up at the SARS review clinic. These cases included patients who were severely ill at presentation, as well as those who presented to the ED at an early stage of the illness. The prevalence of SARS in this setting was 13.3%.

The objectives of this study were:

1. To calculate the sensitivity, specificity, predictive values, and likelihood ratios of chest radiography in predicting SARS, as used in an ED-based screening clinic during a community outbreak;
2. To study the duration in days (i) since onset of symptoms and (ii) since initial presentation for plain chest radiography to develop abnormal changes consistent with SARS;
3. To report the yield and performance of chest radiography from screening patients who presented (i) without fever (temperature not exceeding 37.5°C) and (ii) with temperature not exceeding 38°C.

2. Methods

2.1. Study design

This was a retrospective cohort study of the use of ED plain chest radiography in the diagnosis of SARS. All patient information remained confidential. The chief executives and associated institutional review boards of the Hospital Authority of Hong Kong and of the Prince of Wales Hospital approved the collection of clinical data for surveillance, analysis, research, and reporting.

2.2. Study setting and population

The study was performed on all patients who attended the SARS screening clinic based in the ED of a 1400-bed university teaching hospital, during the outbreak in Hong Kong from March 10 to June 5, 2003. Patients during the early part of this period were triaged for assessment at the screening clinic (a designated section of the ED) if they had respiratory tract symptoms, influenza-like illness, or fever, together with a contact history. During the later stages, when the outbreak had become more widespread in Hong Kong, patients with the above-mentioned symptoms, even without a definite contact history, were triaged for assessment at the clinic. Patients were followed up at the clinic every 1 to 3 days until either hospitalization was required or until follow-up was no longer necessary because of satisfactory resolution of symptoms. Serial frontal chest radiography was performed at follow-up visits.

2.3. Data collection

Patients' medical records from the ED were retrieved and reviewed by a research nurse who extrapolated clinical and demographic details into a database. The record of patients' body temperature during attendance was included in the collation.

2.4. Interpretation of radiographs

Every ED chest film was retrospectively read by 2 of 3 radiologists (W-HN, P-NC, and K-KS) who were blinded to all clinical records. The radiologists had knowledge of the dates when the radiographs were taken and were allowed to evaluate serial chest films of each patient chronologically.

Table 1 The performance of the initial chest radiograph in diagnosing SARS

	SARS	Non-SARS	Total number of patients
Test (chest radiography) positive	True positive (A) = 88	False positive (B) = 55	With positive radiograph (A + B) = 143
Test (chest radiography) negative	False negative (C) = 87	True negative (D) = 1043	With negative radiograph (C + D) = 1130
Total number of patients	With SARS (A + C) = 175	Non-SARS (B + D) = 1098	(A + B + C + D) = 1273

Sensitivity = A/A + C = 50.3%.
Specificity = D/B + D = 95.0%.

Table 2 The performance of serial chest radiography in diagnosing SARS

	SARS	Non-SARS	Total number of patients
Test (chest radiography) positive	True positive (A) = 167	False positive (B) = 67	With positive radiograph (A + B) = 234
Test (chest radiography) negative	False negative (C) = 10	True negative (D) = 1034	With negative radiograph (C + D) = 1044
Total number of patients	With SARS (A + C) = 177	Non-SARS (B + D) = 1101	(A + B + C + D) = 1278

Sensitivity = A/A + C = 94.4%.
Specificity = D/B + D = 93.9%.

The presence of airspace opacification was regarded as test positive for SARS. Using a structured pro forma, the 2 radiologists reported in consensus whether each radiograph was normal, suspicious, or positive. After the review of serial chest radiographs of each patient, the overall impression was also reported.

2.5. Outcome measure

The final diagnosis of SARS was based on the official list of patients recorded in the Hong Kong Department of Health's SARS registry. This list had been prepared by public health experts in Hong Kong, according to the recommendations of the World Health Organization on interpretation of laboratory results for the diagnosis of SARS. The SARS-associated coronavirus (SARS-CoV) antibody status of these patients (immunoglobulin G levels measured by immunofluorescence assay) was also documented for reference.

2.6. Data interpretation and analysis

Descriptive statistics were generated. The performance of chest radiography was assessed by analyzing (i) the chest radiograph at the initial presentation and (ii) the overall conclusion after review of serial chest radiographs, in correlation with the final diagnosis. Reports that were suspicious were regarded as indeterminate and excluded from the analyses. Data were analyzed using Statview for Windows version 5.0 Statistical Analysis Software (Abacus Concepts, SAS Institute, Cary, NC) and MedCalc version 7.0 (MedCalc, Belgium).

3. Results

There were a total of 1378 consecutive patients during the study period. Fifty patients (3.6%) were excluded because their chest radiographs were unavailable for radiologists' review. Of 1328 cases included for analysis, 38.7% were males and 61.3% females. The mean (SD) age was 38.4 (17.0) years. There were 177 cases with final diagnosis of SARS, and the prevalence in this setting was thus calculated to be 13.3%. The SARS-CoV antibody status was positive in 171 patients (96.6%) of those diagnosed with SARS in our study.

The reports on the initial chest radiograph were indeterminate in 55 patients (4.1%). After excluding these from the analysis, the initial chest radiograph had a sensitivity of 50.3% (95% confidence interval [CI], 42.6-57.9), specificity of 95.0% (95% CI, 93.5-96.2), positive likelihood ratio of 10.06, negative likelihood ratio of 0.52, positive predictive value of 61.5%, negative predictive value of 92.3%, and an accuracy of 88.8% for predicting SARS (Table 1).

The reports on serial chest radiography were indeterminate in 50 patients (3.7%). After excluding these from the analysis, serial chest radiography had a sensitivity of 94.4% (95% CI, 89.9-97.3), specificity of 93.9% (95% CI, 92.3-95.3), positive likelihood ratio of 15.48, negative likelihood ratio of 0.060, positive predictive value of 71.4%, negative predictive value of 99.0% , and an accuracy of 93.9% for predicting SARS (Table 2).

Table 3 The performance of serial chest radiography in identifying SARS in patients who presented with a temperature (i) ≤37.5°C and (ii) ≤38°C

	Presenting temperature ≤37.5°C	Presenting temperature ≤38°C
Disease prevalence	9.1%	10.8%
Sensitivity (%)	90.7% (95% CI, 81.7%-96.1%)	92.8% (95% CI, 86.3%-96.8%)
Specificity (%)	96.0% (95% CI, 94.4%-97.3%)	95.6% (95% CI, 94.1%-96.9%)
Positive likelihood ratio	22.79	21.27
Negative likelihood ratio	0.010	0.08
Positive predictive value (%)	69.4	72.0
Negative predictive value (%)	99.0	99.1

For patients who have SARS with positive radiograph (n = 167), the mean (SD) duration from onset of symptoms to positive radiograph was 5.8 (5.4) days. Seventy-nine (47.3%) of these patients had negative or indeterminate chest radiographs at initial presentation, and the mean (SD) duration from initial presentation to positive chest radiograph was 5.4 (6.3) days.

Of 829 patients who initially presented with a temperature of 37.5°C or lower, serial chest radiographs identified 98 (11.8%) positive cases. Of these, 68 (69.4%) were finally diagnosed with SARS. Of 1028 patients who initially presented with a temperature of 38°C or lower, serial radiographs identified 143 (13.9%) positive cases. Of these, 103 (72.0%) were finally diagnosed with SARS. The performance of serial chest radiography in identifying SARS in these 2 categories of cases is shown in Table 3.

4. Discussion

The resurgence of SARS and its propensity to spread rapidly across international borders continue to cause concern for public health authorities worldwide. Recent cases linked to exposures at research laboratories have prompted concerns particularly to countries with laboratories working with live SARS-CoV. The US Centers for Disease Control and Prevention continues to update its guidelines and recommendations for the clinical evaluation of possible SARS-CoV disease [23]. Much has already been published about the etiology, diagnosis, clinical features, and treatment of this illness. Several authors investigated the early predictors of SARS in the ED setting [1,3,22], whereas others have reported the derivation and validation of symptom scores or prediction rules [2,4,5]. The chest radiographic features of SARS have also been extensively studied, and the most consistent initial sign is reported to be airspace opacities or shadowing [7-22]. Radiographic evidence is also an essential element of the case definition [24]. Most authorities would regard the chest radiograph as a very sensitive screening test for diagnosing SARS. However, unfortunately, most studies were based on patients who were already hospitalized, with a high probability of the diagnosis [7,9,12-16,18-20]. Very few looked at the use of chest radiography as an independent screening test in the ED setting, and few were able to report its performance objectively. Only by studies directed at the screening level can full details about "true negatives" and "false negatives" of the test be captured. For those investigators who did study at the screening setting, their studies were limited by the fact that chest radiographs were read by ED physicians who were not blinded to clinical details [1-4]. Therefore, despite the use of multivariate analyses to identify independent associations, their results need to be interpreted with the understanding that any merit identified for the accuracy of chest radiography might have been exaggerated because radiographs were interpreted with a beneficial knowledge of the patients' clinical status. As far as we are aware, our study was the first to investigate the performance of chest radiography as an independent diagnostic test.

Our study found that the sensitivity (50.3%) of the initial chest radiograph was much lower than most authorities would expect. This result has important practical implications. Clinicians ought to be careful not to be falsely reassured by an initially negative chest film. The false-negative rate is high in this setting. Previous anecdotal reports suggested that the chest radiograph could be normal at first presentation [25]. Our results confirmed this possibility, and we report the incidence of its occurrence at our ED screening clinic (Table 1). In contrast, the sensitivity of serial chest radiography in our study was 94.4%, which is a marked improvement from the former. Only by close follow-ups with serial chest radiography and clinical reassessment can the condition be more confidently excluded. Hence, our study lends evidence to the statement that chest radiography is highly sensitive for SARS, but only in the context of interpretation of serial radiographs, instead of the initial screening chest film. The negative predictive value (the probability that the patient is disease-free if the test is negative) of serial chest radiography was 99.0%. The negative likelihood ratio of 0.06 also shows that it is a strong negative predictor. Serial chest radiography is thus extremely useful in ruling out SARS in the setting of a community outbreak.

It is also important to be aware of the specificity of chest radiography for predicting SARS in this setting. The initial radiographic appearance of SARS is not readily distinguishable from pneumonia caused by other etiologic agents [8]. Earlier reports suggest that the changes associated with SARS more commonly involve the lower zone and peripheral lung fields, and that features of cavitation, lymphadenopathy, and pleural effusion are rare [8,12,16-19]. However, the initial appearance and distribution of the airspace disease is also reported to be highly variable, and may be normal, unifocal, multifocal, bilateral, or even extensive [8,12-14,18,19]. Moreover, the cause of airspace opacification is not limited to infection. It may also be caused by the presence of fluid, such as in pulmonary edema. Because patients with clinical and radiographic evidence of SARS require hospitalization with full isolation measures, a low specificity (high false-positive rate) at the screening level would likely result in rapid overwhelming of the hospital system. Few of the earlier studies were able to report on the specificity of chest radiography because few were conducted at the screening level, with a database inclusive of the "true-negative" cases. The specificity is dependent upon the prevalence of other causes of pneumonia during the study period. Nevertheless, our study demonstrated that, despite the concerns mentioned above, the specificity of chest radiography under our setting was excellent, being above 90% for both the initial radiograph and serial chest radiography. The positive likelihood ratio for serial chest radiography was 15.48, showing that it is a

strong positive predictor, capable of generating conclusive changes in post-test probability.

Furthermore, our study revealed that there was considerable yield in screening afebrile patients, or patients with low-grade fever, with serial chest radiography. The 2 temperature cutoffs of 37.5°C and 38°C were chosen for analyses because these values were most often taken as inclusion criteria for triage to "fever clinics" or "SARS screening clinics" in many institutions around the world during the outbreak. Certain recently published prediction rules or novel scoring systems for SARS screening are only applicable to febrile patients with temperatures above 38°C [2,4,5,26]. Our findings show that relying only on these prediction rules would result in a substantial proportion of missed cases (those with temperature not exceeding 38°C) that are identifiable by chest radiography. Our findings provide further evidence to support the current Centers for Disease Control and Prevention recommendation that, when person-to-person transmission is occurring in the world, a patient with contact history who develops respiratory symptoms, even if afebrile, should promptly undergo screening inclusive of chest radiography [23].

5. Limitations

Our study was limited in that it was retrospective in design, and 3.6% of patients were excluded from the study because of the unavailability of radiographs. Nevertheless, the recall bias generally associated with retrospective studies did not affect data collection for the core parameters (the radiologists' report and the final diagnosis) of our study. The patients' body temperatures at presentation were also objectively charted. Our results may not be reproducible at other settings for a number of reasons. First, the prevalence of SARS at other settings may be different. The prevalence of other causes of pneumonia may also have geographic or seasonal variation. A notable example is the increased prevalence of influenza pneumonia during the winter period. This would theoretically affect the specificity of chest radiography, a concern already discussed above. Second, the radiologists who interpreted our radiographs were all specialists, Fellows of the Royal College of Radiologists. By contrast, in practice, chest radiographs in most ED settings are usually read by ED physicians. We do not believe, however, that this would cause significant difficulty in generalizing our results. Finally, our result applies to an ED screening setting during a community outbreak of SARS, with a disease prevalence of 13.3%. It may not be extrapolated to other settings.

6. Conclusions

In conclusion, our study shows that, in the setting of a community outbreak, serial chest radiography is extremely useful as a screening tool in ruling out SARS. However, the chest radiograph at initial presentation performs poorly as a screen, and practitioners are cautioned against overreliance on it to rule out SARS. Conversely, both the initial radiograph and serial radiography are highly specific for SARS in our setting and are therefore excellent in ruling in the disease. Radiographic changes of SARS may precede fever, and the use of chest radiography for screening should not be limited to febrile patients.

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