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Citation	Hong Kong Medical Journal, 2008, v. 14 suppl. 5, p. 8-10
Issued Date	2008
URL	http://hdl.handle.net/10722/151668
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A clinical prediction rule for diagnosing severe acute respiratory syndrome in the emergency department

Key Messages

1. Several features increased the likelihood of severe acute respiratory syndrome (SARS): previous contact with a patient with SARS, fever, myalgia (muscle aches), malaise (feeling unwell), abnormal chest radiograph, and abnormal lymphocyte and low platelet counts. Age older than 65 years or younger than 18 years, sputum production, abdominal pain, sore throat, runny nose, and high neutrophil count decreased the likelihood of SARS.
2. We derived a risk index that used data easily obtained in emergency departments, and identified patients with low and high likelihood of SARS during an outbreak.
3. Study data were obtained by reviewing medical records. Some patients may have had symptoms and findings that were not recorded in the records. Characteristics that identify patients with a high likelihood of SARS may differ in settings that are not large outbreaks.

Hong Kong Med J 2008;14(Suppl 5):S8-10

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RFCID project number: 01030362

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Introduction

Severe acute respiratory syndrome (SARS) was a disease that affected many countries, with more than 8000 cases reported globally, and carried with it a substantial morbidity and high case mortality.[1] It appears unlikely that SARS can be effectively eradicated after the 2003 global epidemic and conceivably it has achieved endemicity in various regions in southern China and elsewhere.

We sought to develop a clinical prediction rule for diagnosis that would accurately identify patients with SARS in the emergency department setting during an outbreak, and to validate the predictive accuracy of this rule.

Methods

This study was conducted from June 2004 to February 2005.

Study design

Retrospective analysis of patient records from two hospitals in Hong Kong using a two-step coefficient-based multivariable logistic regression scoring method, with internal validation by bootstrapping.

Sample size

A total of 2649 patients seen at two Hong Kong triage clinics during the 2003 SARS epidemic were studied. There were 1274 ($n_{non\text{-}SARS}$=897, n_{SARS}=377) consecutive patients from the United Christian Hospital, and 1375 ($n_{non\text{-}SARS}$=1191, n_{SARS}=184) consecutive patients from the Prince of Wales Hospital.

Study instruments

We reviewed medical records of these patients who visited SARS triage clinics in the emergency departments of these two Hong Kong hospitals in 2003. Specifically, we reviewed standard forms that had been used to record patient symptoms at the presentation, physical findings, chest radiography, and blood laboratory results. We also reviewed records to see which patients had blood test results that confirmed SARS. We analysed these data to determine which presenting features were associated with increased and decreased probabilities of diagnosing SARS. Then, we used a risk index to score characteristics that helped identify or rule out SARS, and tested the ability of the risk index to correctly identify SARS patients.

Main outcome measures

Points were assigned on the basis of history, physical examination, and simple investigations obtained at presentation. The outcome measure was a final diagnosis of SARS, as confirmed by World Health Organization laboratory criteria.

Results

Several features increased the likelihood of SARS—previous contact with a patient with SARS, fever, myalgia (muscle aches), malaise (feeling weak), abnormal chest radiograph, and abnormal lymphocyte and low platelet counts. Age older than 65 years or younger than 18 years, sputum production, abdominal

Table 1. Multivariable predictors of SARS diagnosis and associated risk scoring system for step 1

Characteristic	Points assigned*	Beta regression coefficient (95% confidence interval) $n_{estimation,\ step1}$=2039
Age-group (years)		
<18	-1	-0.15 (-0.55 to 0.25)
18-64	0	Reference
≥65	-5	-0.81 (-1.21 to -0.41)
Contact history		
Yes	8	1.14 (0.86 to 1.42)
No	0	Reference
Presence of symptoms on presentation		
Fever	15	2.18 (1.83 to 2.53)
Myalgia	3	0.40 (0.13 to 0.67)
Malaise	3	0.47 (0.21 to 0.72)
Sputum production	-4	-0.63 (-0.94 to -0.32)
Abdominal pain	-8	-1.24 (-1.82 to -0.66)
Sore throat	-5	-0.67 (-0.98 to -0.37)
Rhinorrhoea	-4	-0.55 (-0.87 to -0.23)

* Cutoff threshold for total point score (with a pre-specified sensitivity of 0.99: ≥ –3 indicates high-risk group whereas < –3 indicates low-risk group

Table 2. Multivariable predictors of SARS diagnosis and associated risk scoring system for step 2

Characteristic	Score assigned*	Beta regression coefficient (95% confidence interval) $n_{estimation,\ step2}$=1053
Age-group (years)		
<18	-1	-0.25 (-0.86 to 0.36)
18-64	0	Reference
≥65	-6	-1.54 (-2.13 to -0.94)
Contact history		
Yes	7	1.66 (1.20 to 2.13)
No	0	Reference
Fever	5	1.32 (0.82 to 1.83)
Sputum production	-4	-0.91 (-1.34 to -0.48)
Chest X-ray		
Normal	0	Reference
Haziness	8	1.91 (1.45 to 2.36)
Pneumonia (unilateral lesion, bilateral lesion)	8	1.98 (1.39 to 2.56)
Lymphocyte count ($x10^9$/L)		
Low (<1.5)	5	1.29 (0.89 to 1.70)
Normal (1.5-4)	0	Reference
High (>4)	5	1.24 (-0.81, 3.29)
Neutrophil ($x10^9$/L)		
Low (<2.0)	4	0.98 (0.073, 1.88)
Normal (2.0-7.5)	0	Reference
High (>7.5)	-5	-1.29 (-1.79, -0.79)
Platelets ($x10^9$/L)		
Low (<150)	5	1.16 (0.70, 1.61)
Normal (150-400)	0	Reference
High (>400)	-5	-1.12 (-2.87, 0.62)

* Cutoff threshold for total point score (with a pre-specified sensitivity of 0.95: ≥8 indicates high-risk group whereas <8 indicates low-risk group

pain, sore throat, runny nose, and high neutrophil count decreased the likelihood.

In step 1 of the clinical prediction rule, age in years (18-64 vs ≥65) and contact history were independently associated with a final diagnosis of SARS. In addition, the presence of three cardinal symptoms (fever, myalgia, and malaise) and the absence of sputum production, abdominal pain, sore throat, and rhinorrhoea were each independently associated with a final diagnosis of SARS (Table 1). None of the vital signs achieved statistical significance in the stepwise multivariable model and were therefore excluded. A total of 11% of the cohort with a total score of less than the threshold of -3 was assigned to the low-risk group, and did not proceed to step 2.

In step 2, in addition to four of the nine factors identified in step 1, four radiographic/laboratory findings (chest radiograph, lymphocyte count, neutrophil count, and platelet count) were each independently associated with a final diagnosis of SARS. Myalgia, malaise, abdominal pain, sore throat, and rhinorrhoea no longer achieved statistical significance in step 2 after inclusion of the investigations. The point scoring system shown in Table 2 was used to quantify the magnitude of association of each of these eight factors with SARS. A total score of 8 or greater would qualify the patient as being at high risk for SARS, with a pre-specified sensitivity of 95% overall. A total of 8% of

those considered in step 2 were further assigned to the low-risk category.

Using an internal validation procedure, application of the rule achieved an optimism-corrected sensitivity of 0.90, a specificity of 0.62, and an area under the receiver-operating characteristics (ROC) curve of 0.85.

Discussion

Our findings suggest that a simple model that uses clinical data at the time of presentation to an emergency department during an acute outbreak can predict the incidence of SARS and provide a practical diagnostic decision aid. The clinical prediction rule achieved high sensitivity and area under the ROC curve, which were maintained on internal validation by bootstrapping. This finding is important because of the high case-fatality ratio of SARS and potential public health hazards associated with its misdiagnosis. In addition, the rule could rule out SARS in a substantial proportion of persons presenting to an emergency department.

Ma et al[2] validated our rule on SARS data from Taiwan and showed that our rule performed very well, with a sensitivity of 98.8%, and a specificity of 52.0%. These results confirm the generalisability of the algorithm beyond Hong Kong to another urban population affected by SARS.

Before recommending the adoption of this clinical prediction rule by public health authorities in their SARS management plans, we must address several potential limitations. First, the analysis was based on data from retrospective chart review, and, therefore, the accuracy and completeness of information, as documented in the medical records, would influence the validity of the results.

Second, this rule was derived by using data from an acute outbreak; in this situation, the prevalence of SARS at the time of presentation was very high. Therefore, the prediction rule may not apply to isolated cases during the interepidemic period.

Third, the rule was constructed from dichotomous or categorical variables to facilitate use in practice. This may oversimplify the way physicians interpret the predictor variables. Therefore, as with all clinical practice guidelines, our rule should not supersede the physician's judgement in equivocal or borderline cases.

On a more practical level, health care providers should remember the usual limitations associated with practice guidelines and must maintain a high level of clinical suspicion, especially in the case of SARS and when isolation wards can still cope with admitting more patients. This decision tool will be most useful in a large epidemic when the health system's surge capacity is being overwhelmed by the number of patients seeking care.

Ultimately, the generalisability of the findings should be validated further prospectively, if SARS returns. In the meantime, we believe our prediction rule will provide the best evidence-based guidelines for the triage and management of patients suspected to have SARS when presenting to emergency departments and primary care settings.

Acknowledgements

This study was supported by the Research Fund for the Control of Infectious Disease, Food and Health Bureau, Hong Kong SAR Government (RFCID: 01030362), an RFCID Commissioned Study grant to the University of Hong Kong, and the University of Hong Kong SARS Research Fund. We are indebted to the colleagues in the Accident and Emergency Departments of Pamela Youde Nethersole Eastern Hospital, Prince of Wales Hospital, and United Christian Hospital. We also thank Dr Wing-nam Wong for data capture, entry, and cleaning; staff in the Health Informatics, Information Technology, Medical Services Development, and Statistics Divisions of the Hospital Authority Head Office for collating and processing multiple data sources used in this analysis.

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