



Original Contribution

Clinical prediction rule to predict pneumonia in adult presented with acute febrile respiratory illness

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ABSTRACT

Objective: To derive a clinical prediction rule to predict pneumonia in patients with acute febrile respiratory illness to emergency departments.

Method: This was a prospective multicentre study. 537 adults were recruited. Those requiring resuscitation or were hypoxaemic on presentation were excluded. Pneumonia was defined as new onset infiltrates on chest X-ray (CXR), or re-attendance within 7 days and diagnosed clinically as having pneumonia. A predictive model, the Acute Febrile Respiratory Illness (AFRI) rule was derived by logistic regression analysis based on clinical parameters. The AFRI rule was internally validated with bootstrap resampling and was compared with the Diehr and Heckerling rule.

Results: In the 363 patients who underwent CXR, 100 had CXR confirmed pneumonia. There were 7 weighted factors within the AFRI rule, which on summation, gave the AFRI score: age ≥ 65 (1 point), peak temperature within 24 h ≥ 40 °C (2 points), fever duration ≥ 3 days (2 points), sore throat (−2 points), abnormal breath sounds (1 point), history of pneumonia (1 point) and SpO₂ $\leq 96\%$ (1 point). With the bootstrap resampling, the AFRI rule was found to be more accurate than the Diehr and Heckerling rule (area under ROC curve 0.816, 0.721 and 0.566 respectively, $p < 0.001$). At a cut-off of AFRI ≥ 0 , the rule was found to have 95% sensitivity, with a negative predictive value of 97.2%. Using the AFRI score, we found CXR could be avoided for patients having a score of < 0 .

Conclusion: AFRI score could assist emergency physicians in identifying pneumonia patients among all adult patients presented to ED for acute febrile respiratory illness.

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1. Introduction

Numerous patients attend emergency departments (EDs) for fever and respiratory tract symptoms. A subset of them would be suffering from pneumonia instead of simple upper respiratory tract infection. Pneumonia is a common disease presenting to emergency departments; the reported incidence of patients coughing with underlying pneumonia is up to 27% [1,2]. Emergency physicians are challenged to distinguish pneumonia from upper respiratory tract infections in febrile patients with acute respiratory tract symptoms. Whilst latter may simply be self-limiting, the former may progress with serious complications [3].

Unfortunately, symptoms and signs of pneumonia overlap significantly with simple upper respiratory tract infection [4,5]. It was

shown that no single symptom or vital sign can reliably distinguish them [1,8–10]. Furthermore, individual physicians may also weigh symptoms or physical signs differently [6–8]. Chest X-ray (CXR) is often utilized [7,11]. However, liberal ordering of CXR exposes individuals to unnecessary radiation. While experienced clinicians may better use their clinical skills to determine the necessity of ordering a CXR, a risk stratifying prediction rule may assist all emergency physicians in whether a CXR should be ordered with better consistency and reproducibility.

The possibility of predicting pneumonia from clinical parameters was studied by a number of researchers in the literature [2,9,12–16]. They derived an association between the diagnosis of pneumonia and its presenting symptoms and physical signs, using an abnormal CXR as confirmation of the diagnosis. Another approach was to use a model to rule out pneumonia but this was found unsatisfactory [16]. Most of them are retrospective studies.

We conducted a multicentre prospective study to determine clinical predictors of the disease pneumonia, based on a number of bedside

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parameters in adults presenting with an acute febrile respiratory tract illness.

1.1. Objective

The objective of this study is to evaluate independent determinant factors in prediction of pneumonia and establish a clinical prediction rule for pneumonia in adult patients with acute febrile respiratory illness. The primary objective is to derive a clinical prediction rule to predict pneumonia in adults presenting to the ED with acute febrile respiratory illness, with implication of reduction of Chest X-rays required with a low risk criteria. The secondary objective is to identify a high-risk group of pneumonia which would have implication in earlier assessment in triage.

2. Methods

2.1. Study setting and design

This was a multi-centre prospective cohort study. The EDs of 3 public hospitals in Hong Kong, namely Tuen Mun Hospital, Princess Margaret Hospital, and Pok Oi Hospital participated in the study. Tuen Mun Hospital has over 600 attendances daily, while Pok Oi Hospital and Princess Margaret Hospital averages at 350 cases daily.

2.2. Subject recruitment

From September 2016 to May 2017, patients age ≥ 18 years who presented to ED with temperature ≥ 38 °C over the preceding 24 h, and an acute onset of respiratory tract symptoms within 10 days from attendance were included. The body temperature could be triage-measured or patient-reported temperature, measured either through oral, rectal or tympanic routes. Respiratory tract symptoms included cough, dyspnoea, wheezing and added sounds during respiration. Hypoxaemic patients with oxygen saturation levels (SpO₂) $\leq 94\%$ detected by oximetry, those requiring oxygen supplementation or immediate resuscitation were excluded. Pneumonia, was defined as new onset of pulmonary infiltrate or consolidation in CXR, or re-attendance to any hospital ED within 7 days and subsequently diagnosed to have pneumonia. All CXRs were evaluated by two independent qualified emergency physicians. If their interpretations differed, adjudication would be sought from an independent radiologist. All previous CXRs were available to all the assessors and radiologists for comparison.

2.3. Data collection

Eligible patients were identified at triage. They were assessed by the emergency physicians in the usual manner. Clinical data including symptoms, vital signs and physical signs were collected using a standardized data collection form. In order to avoid undue influence in their clinical actions, the form implied no guidance or suggestions of any further investigations. The definition of temperature within 24 h included the reported self-measured body temperature within 24 h, or the temperature measured at the triage station, whichever the higher. The decision for imaging was solely made by the clinician at their clinical discretion. The form was only filled at the juncture when clinicians had obtained history, physical signs, and decided the necessity of CXR but before availability of radiographs. This was to minimize reporting variability from different clinicians. All patients suitable for discharge were instructed to reattend if their condition worsened. The completed forms were then collected, the data verified against ED record and entered into the computer system.

2.4. Statistical analysis

Sample size was calculated using the NCSS PASS 2011 software. It was calculated by the binomial logistic regression model with the following assumptions: a power of 80%, level of significance of 5% with the two-tailed hypothesis. Effect size was taken to be the odds ratio of 2. Results of a preliminary survey indicated a prevalence of radiological pneumonia among adult patients attending with fever and respiratory tract symptoms to be 20%. To identify a binomial predictor with odds ratio of 2 or more and a 20% incidence rate, a sample of 511 patients would be required.

The statistical software package employed was IBM SPSS Statistics for Windows, Version 22.0. Armonk, NY: IBM Corp. 2013. Cohen's Kappa was used to assess inter-observer variability for the CXR. Univariate comparison of parameters was conducted for the positive outcome group and the contrary. Continuous parameters were compared by independent sample *t*-test or Mann-Whitney *U* test where appropriate. They were further stratified into different subgroups for comparison. Categorical data was compared with Chi-square test, or Fisher's exact test when one of the cell values was < 5 . We took a $p < 0.05$ value as statistically significant and the 95% confidence interval (CI) was reported.

A model for prediction of pneumonia, the Acute Febrile Respiratory Illness (AFRI rule), was derived by logistic regression with backward stepwise method by likelihood ratio (LR). Weights of predictors were assigned based on the logarithm of the adjusted odds ratios (OR). Model calibration was evaluated by the Hosmer-and-Lemeshow test. Model discrimination was evaluated by the area under receiver operating curve (AUROC) of the predicted probabilities. The sensitivity, specificity, LR were reported for various cut-offs. The AFRI rule was internally validated with bootstrap resampling and the diagnostic performance was compared to the Diehr and Heckerling rule [9,13]. The Diehr rule consisted of 7 parameters: nasal discharge (−2 points), sore throat (−1 point), night sweats (+1 point), myalgia (+1 point), sputum (+1 point), respiratory rate > 25 per minute (+1 point), body temperature ≥ 100 °F (2 points). The points were summed up for the prediction of pneumonia. The Heckerling rule consisted of 5 parameters (body temperature > 100 °F, heart rate > 100 beat per minute, diminished breath sound, crackles, absence of asthma) with 1 point for each and the sum of them being the prediction score.

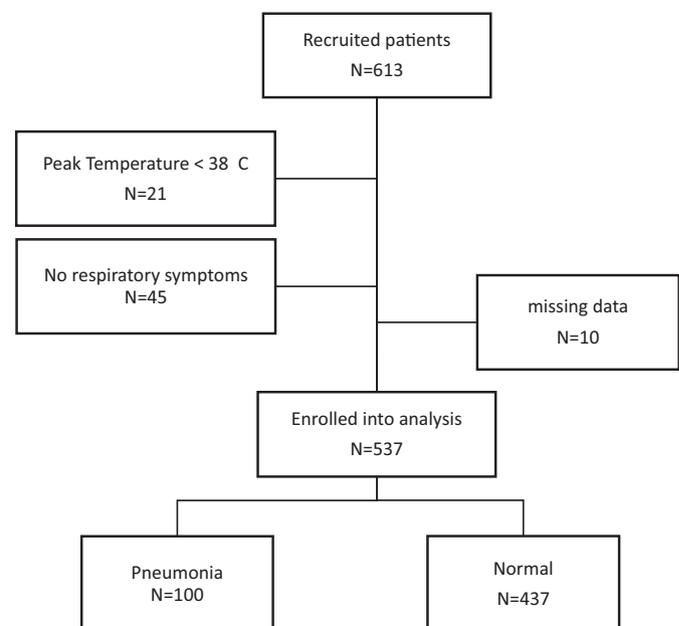


Fig. 1. Patient recruitment.

This study was approved by the institutional research bureaus of the participating hospitals. There was no funding or financial sponsorship. All the investigators reported no conflict of interests.

3. Results

Fig. 1 showed the patient recruitment data. A total of 613 adult patients were recruited, 21 of them were excluded as the peak temperature reported was <38 °C. Forty-five patients were further excluded for the lack of respiratory symptoms and 10 more were excluded because of missing data. In the end 537 patients were enrolled into analysis, of whom 363 patients had a CXR taken. While 100 patients (18.6%) had pneumonia, 97 were diagnosed at first attendance. Five patients re-attended within 7 days, with two of them having radiological features of pneumonia in the initial CXR.

Univariate analysis of the demographics, symptoms and signs was listed in Table 1. There were significant differences between the two groups in age and history of pneumonia. Gender, smoking status,

presence of chronic diseases was not significantly different. Self-reported peak temperature, fever duration, dyspnoea, prior antibiotic treatment was significantly more prevalent in the pneumonia group, while sore throat, nasal symptoms more in the negative group. For vital and clinical signs, there were significantly lower blood oxygen saturation (SpO₂ of $\leq 96\%$) and abnormal breath sounds in those with pneumonia, but the triage measured temperature, pulse rate, blood pressure and respiratory rate (RR) showed no significant difference compared with those without pneumonia. SpO₂ in non-hypoxic range was assessed for association with the probability of pneumonia. Fig. 2 demonstrated that low-normal SpO₂ in non-hypoxic patients was highly predictive of pneumonia.

Good agreement was demonstrated between the two independent assessors of the CXRs. Observer agreement was found in 354 of 363 patients who had CXRs (97.5%). Cohen's Kappa value was 0.936.

The association of SpO₂ in non-hypoxic range was assessed for the probability of pneumonia.

Table 1
Univariate analysis of demographics, symptoms and signs.

	All (n = 537)	Positive outcome (n = 100)	Negative outcome (n = 437)	P value
Demographic and outcome				
Age ≥ 65	151 (28.1%)	48 (48%)	103 (23.6%)	<0.001
Male gender	264 (49.2%)	54 (54%)	210 (48.1%)	0.283
Current smoker	91 (16.9%)	23 (23%)	68 (15.6%)	0.074
Alcohol abuse	5 (0.9%)	3 (3%)	2 (0.5%)	0.047
Institutionalized	27 (5%)	8 (8%)	19 (4.3%)	0.132
Brought in by ambulance	127 (23.6%)	39 (39%)	88 (20.1%)	<0.001
Past history				
Past history of pneumonia	88 (16.4%)	30 (30%)	58 (13.3%)	<0.001
Past history of tuberculosis	18 (3.4%)	4 (4%)	14 (3.2%)	0.757
Asthma	18 (3.4%)	4 (4%)	14 (3.2%)	0.757
Chronic lung diseases	23 (4.3%)	8 (8%)	15 (3.4%)	0.042
Immunocompromised/on immunosuppressant	8 (1.5%)	2 (2%)	6 (1.4%)	0.646
Diabetes mellitus	65 (12.1%)	16 (16%)	49 (11.2%)	0.186
Malignancy	33 (6.1%)	10 (10%)	23 (5.3%)	0.075
Symptoms				
Peak temperature within 24 h ≥ 40 °C	30 (5.6%)	10 (10%)	20 (4.6%)	0.033
Fever duration ≥ 3 days	161 (30%)	48 (48%)	113 (25.9%)	<0.001
Chills	235 (43.8%)	47 (47%)	188 (43%)	0.469
Cough	522 (97.2%)	98 (98%)	424 (97%)	1.000
Purulent sputum	151 (28.1%)	35 (35%)	116 (26.5%)	0.09
Feeling dyspnoeic	120 (22.3%)	41 (41%)	79 (18.1%)	<0.001
Noisy breathing	26 (4.8%)	6 (6%)	20 (4.6%)	0.553
Sore throat	286 (53.3%)	21 (21%)	265 (60.6%)	<0.001
Nasal blockage/discharge	319 (59.4%)	39 (39%)	280 (64.1%)	<0.001
Abdominal pain	23 (4.3%)	2 (2%)	21 (4.8%)	0.28
Nausea	39 (7.3%)	4 (4%)	35 (8%)	0.202
Vomiting	55 (10.2%)	8 (8%)	47 (10.8%)	0.412
Diarrhoea	27 (5%)	2 (2%)	25 (5.7%)	0.201
Received antibiotic within 7 days	71 (13.2%)	24 (24%)	47 (10.8%)	<0.001
Presenting vital signs				
Temperature, °C [median \pm IQR]	38.1 (37.2–38.6)	38 (37–38.5)	38.1 (37.3–38.6)	0.783
Temperature ≥ 38 °C	311 (57.9%)	60 (60%)	251 (57.4%)	0.64
Temperature ≥ 39 °C	71 (13.2%)	10 (10%)	61 (14%)	0.292
Temperature ≥ 40 °C	3 (0.6%)	1 (1%)	2 (0.5%)	0.462
Pulse rate, beats per min [mean \pm SD]	102 \pm 18	102 \pm 17	102 \pm 19	0.688
Pulse rate > 120 /min	117 (21.8%)	20 (20%)	97 (22.2%)	0.631
Systolic blood pressure, mm Hg [mean \pm SD]	136 \pm 23	139 \pm 25	135 \pm 23	0.313
Diastolic blood pressure, mm Hg [mean \pm SD]	77 \pm 14	76 \pm 14	77 \pm 14	0.152
Respiratory rate, breaths per min [median \pm IQR]	18 (16–18)	18 (16–20)	18 (16–18)	0.359
Respiratory rate > 16 /min	223 (41.5%)	53 (53%)	170 (38.9%)	0.149
Respiratory rate > 20 /min	51 (9.5%)	14 (14%)	37 (8.5%)	0.239
Respiratory rate > 24 /min	20 (3.7%)	5 (5%)	15 (3.4%)	0.587
SpO ₂ $\leq 96\%$	130 (26.9%)	41 (43.2%)	89 (22.9%)	<0.001
Physical examination				
Crackles, reduced or bronchial breath sounds	7 (1.3%)	5 (5%)	2 (0.5%)	0.003
Wheeze on examination	30 (5.6%)	10 (10%)	20 (4.6%)	0.033
Abnormal breath sounds	70 (13%)	31 (31%)	39 (8.9%)	<0.001

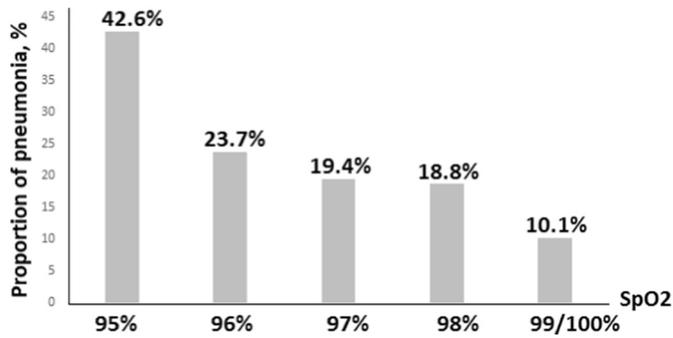


Fig. 2. Association between SpO2 and probability of pneumonia.

3.1. The Acute Febrile Respiratory Illness (AFRI) rule

Table 2 showed the selected independent predictive factors. They were assigned points with reference to the logarithm of the adjusted odds ratio. The AFRI score was obtained by adding all the points. The characteristics of the AFRI rule at various cut-offs were presented in Table 3. At a cut-off of AFRI ≥ 0 , the rule had 95% sensitivity, while at cut-off of AFRI ≥ 3 , specificity of AFRI rule was 90.2%.

The AUROC of the AFRI rule with bootstrapping resampling validation ($k = 1000$) was presented in Fig. 3. Compared with existing models, AFRI had AUROC of 0.816 (CI 0.780–0.848; $p < 0.001$), while that of Diehr being 0.721 (CI 0.681–0.759; $p < 0.001$), Heckerling 0.566 (CI 0.523–0.608; $p = 0.055$). Thus, the AFRI rule had overall better sensitivity and specificity.

4. Discussion

In our study, we demonstrated that it was possible to predict pneumonia from readily measurable bedside parameters and clinical symptoms and signs. In line with other literature, we have demonstrated age, temperature, abnormal breath sounds and history of pneumonia significantly increased the odds of having pneumonia [2,9,12–15]. The presence of chronic lung diseases, immunocompromised state was not significant predictors [9]. However, the number of such cases in our cohort might be too small to detect such an association. Exclusion of unstable and hypoxaemic cases might also be a factor in selection bias against such an association.

Apart from the presence of fever, we found that the duration of fever and peak temperature were important predictors. Both were not reported in previous studies [2,9,12–15]. Interestingly, the self-reported peak body temperature within 24 h was a more significant predictive factor than the triage measured temperature. *This might be reflective of the body's pyretic response to sepsis.* Our postulation would be more vigorous pyretic response in pneumonia compared to simple upper respiratory infection. It would be interesting to see whether this observation holds in paediatric patients.

Table 2
Logistic regression model predicting X-ray confirmed pneumonia and assigned weight in AFRI rule

	Log OR	Wald	Odds ratio (95% CI)	P value	Score
Age ≥ 65	0.831	6.133	2.3 (1.19–4.43)	0.013	1
History of pneumonia	0.717	4.517	2.05 (1.06–3.97)	0.034	1
Peak temperature ≥ 40 °C	1.361	7.453	3.9 (1.47–10.36)	0.006	2
Fever duration ≥ 3 days	1.429	19.44	4.17 (2.21–7.87)	<0.001	2
Sore throat	-1.474	20.636	0.23 (0.12–0.43)	<0.001	-2
Abnormal breath sounds	0.84	6.487	2.32 (1.21–4.43)	0.011	1
SpO2 $\leq 96\%$	0.649	5.328	1.91 (1.1–3.32)	0.021	1

Hosmer-and-Lemeshow goodness-of-fit test $p = 0.078$.

AUROC of predicted probabilities 0.838 (95% CI 0.797–0.879).

Similar to Diehr, we demonstrated that sore throat or nasal symptoms were significant negative predictors of pneumonia. Agents of common cold were known to infect the nasal mucosa in preference to that of the lower respiratory tract. Rhinovirus, in particular, had been shown to have limited potential to invade the bronchial mucosa and alveoli [5]. The predominance of upper respiratory tract symptoms might signify the pathogenic agent exerting its virulence in the nose and throat but not the lower respiratory tract. The presence of these symptoms may therefore indicate the probability of a common cold rather than pneumonia.

We found an association between reduced arterial oxygen tension without frank hypoxaemia and the risk of pneumonia. The chance of pneumonia in patients with SpO2 of 95% was 4 times higher than the group with 99–100% on room air. With pneumonia, the lung parenchyma becomes acutely inflamed. There is migration of neutrophils into pulmonary air spaces, together with exudates, causing lung consolidation [17]. There is arteriovenous shunting and ventilation-perfusion mismatch which may be causing the observed small drop in SpO2 reading. Fig. 2 shows the inverse association between falling SpO2 values and cases of pneumonia diagnosed, especially when the SpO2 fell below 96%. even after confounding factors were controlled (OR 1.91, $p < 0.021$). It would therefore appear that even a subtle drop in SpO2 value was associated with pneumonia. Our higher cut-off value of SpO2 in the AFRI rule might be explained by the fact we excluded the hypoxaemic patients, reflected by the mean SpO2 of our cohort being 98%. This result might also be facilitated by the advances of modern oximeters being more precise to detect true subtle SpO2 changes [18,19]. We did not demonstrate an association between heart rate and incidence of pneumonia found in previous studies [2,12–14]. *The exclusion of the sickest hypoxaemic patients might have reduced the apparent association between tachycardia and the presence of pneumonia.*

We did not find respiratory rate (RR) a predictive factor for pneumonia [2,12,20]. While RR is an objective measurement, its counting accuracy may be limited within the busy environment of the ED, especially when techniques such as “spot assessment” in place of actual counting can be practiced [21,22]. RR was not statistically significant in our model and its practicability was thus limited. However, this difference with previous studies was not detrimental to the usefulness of the AFRI rule, considering we adopted a pragmatic approach in the development of our model.

The AFRI rule can be applied readily in the busy ED setting. It has overall better performance as shown by the AUROC. It can be performed in a very short time. Most of the individual predictive factors are objective measurements. Furthermore, different cut-off values for different scenarios can be utilized. The AFRI rule can also be useful for patient triage in the ED. For triage, we propose either a higher patient triage category for early assessment and/or triage-initiated CXR when the AFRI score is ≥ 3 . This would help detect 39% of pneumonia cases while initiating CXR in 15.3% of patients. Using a higher AFRI score for triage initiated CXR, the number of CXRs ordered can be reduced for a lower diagnostic sensitivity but higher specificity. With the latter criteria, 19% of patients with pneumonia would be diagnosed with only 2.7% having an unnecessary CXR. If an AFRI score of ≥ 0 is used, a 95% sensitivity can be achieved. Conversely, a negative AFRI score (i.e., <0) may indicate that a CXR is not required, thus reducing unnecessary tests.

In addition, we propose that the AFRI may be potentially useful in a primary care setting in relation to the decision making for ordering a CXR. This will however need further validation within a primary care setting.

4.1. Limitations

We collected data prospectively to establish the relationship between symptoms, signs and vital parameters in pneumonia. We chose the CXR as a diagnostic reference in our study. The inability to perform CXR in all cases was the major limitation of our study, resulting in

Table 3
Diagnostic characteristics of AFRI rule at various cut-offs

Outcome	AFRI ≥ 0	AFRI ≥ 1	AFRI ≥ 2	AFRI ≥ 3	AFRI ≥ 4	Diehr ≥ 1	Heckerling ≥ 3
Positive prediction	360 (67%)	254 (47.3%)	182 (33.9%)	82 (15.3%)	31 (5.8%)	381 (70.9%)	310 (57.7%)
Positive/negative outcome	95/265	88/166	78/104	39/43	19/12	91/290	64/246
Negative prediction	177 (33%)	283 (52.7%)	355 (66.1%)	455 (84.7%)	506 (94.2%)	156 (29.1%)	227 (42.3%)
Positive/negative outcome	5/172	12/271	22/333	61/394	81/425	9/147	36/191
Sensitivity	95 (88.2–98.1)	88 (79.6–93.4)	78 (68.4–85.4)	39 (29.6–49.3)	19 (12.1–28.3)	91 (83.2–95.5)	64 (53.7–73.2)
Specificity	39.4 (34.8–44.1)	62 (57.3–66.6)	76.2 (71.9–80.1)	90.2 (86.9–92.7)	97.3 (95.2–98.5)	33.6 (29.3–38.3)	43.7 (39–48.5)
PLR	1.57 (1.43–1.71)	2.32 (2.01–2.66)	3.28 (2.69–3.99)	3.96 (2.72–5.77)	6.97 (3.5–13.88)	1.37 (1.25–1.5)	1.13 (0.96–1.35)
NLR	0.13 (0.05–0.3)	0.19 (0.11–0.33)	0.29 (0.2–0.42)	0.68 (0.58–0.79)	0.83 (0.76–0.92)	0.27 (0.14–0.5)	0.82 (0.63–1.08)

verification bias. On the other hand, we considered it an ethical and practical approach in not subjecting all patients to a having CXR. Moreover, the true sensitivity and specificity of CXR in cases of pneumonia is unknown [10,11]. The decision to perform a CXR was thus left to the discretion of the attending emergency physician. As such, some cases of pneumonia could be missed. However, all patients were instructed to return should symptoms persisted or worsened. We were unable to perform follow-up examinations due to limited resources and the burden of follow-up for all discharged patients. The set-up of a composite outcome including re-attendance with a diagnosis of pneumonia was intended to compensate this situation.

Although previous studies showed physicians tended to have wide interobserver variability [23], Emerman et al. [24], had compared physician's judgement and CXR in detecting pneumonia from the 7% of the 290 subjects. Physicians' judgement was found to be more sensitive than prediction rules. However, they tended to order an excess number of CXRs. In our study, we believed the number of missed pneumonia because a CXR was not ordered would be small. The small number of re-attendant patients would support this proposition.

The AFRI rule demonstrated overall better performance than existing rules in the ED. While the rule was derived from 3 local hospitals with different population characteristics, these might not be representative of other districts of Hong Kong. Furthermore, the prevalence of pneumonia differs in different ethnic groups as well. We postulate that the rule could be even more useful in the primary care setting to guide

referral to the ED or performing a CXR. However, we expect the prevalence of pneumonia in primary care patients will differ from those presenting to the ED, and hence the pre-test probability and the predictive values of the AFRI, if used in this setting, may be different. Validation studies of the AFRI rule would therefore be required in other centres, and if feasible, in the primary care setting. Impact analysis and comparison with clinical assessment alone would also be important before the rule can be widely accepted.

5. Conclusion

A combination of symptoms and signs along with a number of vital parameters predicted radiologically confirmed pneumonia on CXR. The AFRI rule is a score derived from the summation of a number of individual predictor scores, based on these symptoms, signs and vital parameters. We demonstrated that the AFRI rule was effective in predicting pneumonia in patients presenting with an acute febrile illness with respiratory tract symptoms. Furthermore, the AFRI rule score can assist in determining the need to proceed with further examination with a CXR, as well as potentially assisting in triage priorities when a patient presents to the ED. We further propose that the threshold score for these to happen could be tailored individually for different EDs, depending on their resource availability and the population they serve.

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Conflict of interest

There was no conflict of interest of each author, in accordance with ICJME guidelines.

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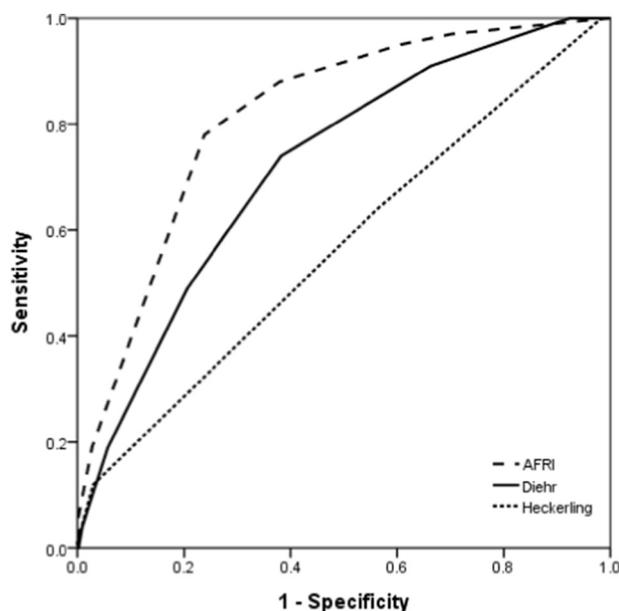


Fig. 3. ROC curves of the AFRI rule, Diehr rule and Heckerling rule CXR confirmed pneumonia with bootstrapping resampling validation ($k = 1000$).

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