ORIGINAL ARTICLE 10.1111/j.1469-0691.2011.03736.x

Severity assessment tools in ICU patients with 2009 Influenza A (H1N1) pneumonia

J. M. Pereira[1], R. P. Moreno[2], R. Matos[2], A. Rhodes[3], I. Martin-Loeches[4], M. Cecconi[3], T. Lisboa[5] and J. Rello[6] on behalf of the ESICM H1N1 Registry Steering Committee and the ESICM H1N1 Registry Contributors*

1) *Intensive Care Department, Hospital S. João EPE, Faculdade de Medicina do Porto, Porto,* 2) *Unidade de Cuidados Intensivos Polivalente, Hospital de Sto António dos Capuchos, Centro Hospitalar de Lisboa Central, E.P.E, Lisboa, Portugal,* 3) *Critical Care Department, St George's Healthcare NHS Trust, London, UK,* 4) *Critical Care Department, Joan XXIII University Hospital, CIBERes Enfermedades Respiratórias IISPV, Tarragona, Spain,* 5) *Critical Care Department, Hospital de Clínicas de Porto Alegre, Porto Alegre, Brazil and* 6) *Critical Care Department, Vall d'Hebron University Hospital, Institut de Recerca Vall d'Hebron, CIBERes, Universitat Autonoma Barcelona, Barcelona, Spain*

Abstract

The aim of this study was to determine if severity assessment tools (general severity of illness and community-acquired pneumonia specific scores) can be used to guide decisions for patients admitted to the intensive care unit (ICU) due to pandemic influenza A pneumonia. A prospective, observational, multicentre study included 265 patients with a mean age of 42 (±16.1) years and an ICU mortality of 31.7%. On admission to the ICU, the mean pneumonia severity index (PSI) score was 103.2 ± 43.2 points, the CURB-65 score was 1.7 ± 1.1 points and the PIRO-CAP score was 3.2 ± 1.5 points. None of the scores had a good predictive ability: area under the ROC for PSI, 0.72 (95% CI, 0.65–0.78); CURB-65, 0.67 (95% CI, 0.59–0.74); and PIRO-CAP, 0.64 (95% CI, 0.56–0.71). The PSI score (OR, 1.022 (1.009–1.034), p 0.001) was independently associated with ICU mortality; however, none of the three scores, when used at ICU admission, were able to reliably detect a low-risk group of patients. Low risk for mortality was identified in 27.5% of patients using PIRO-CAP, but above 40% when using PSI (I–III) or CURB65 (<2). Observed mortality was 13.7%, 13.5% and 19.4%, respectively. Pneumonia-specific scores undervalued severity and should not be used as instruments to guide decisions in the ICU.

Keywords: Critically ill, influenza A (H1N1)v, pneumonia, severity scores, triage
Original Submission: 20 August 2011; **Revised Submission:** 18 November 2011; **Accepted:** 19 November 2011
Editor: M. Paul

Clin Microbiol Infect

Corresponding author: J. M. Pereira, Intensive Care Department, Hospital S. João, E.P.E., Al Prof Hernâni Monteiro, 4200-319 Porto, Portugal
E-mail: jmcrpereira@yahoo.com

*European Society of Intensive Care Medicine (ESICM) H1N1 Registry Contributors are listed in Appendix 1.
Endorsed by the European Critical Care Research Network (ECCRN) of the European Society of Intensive Care Medicine (ESICM).

Introduction

The prevalence of severe community-acquired pneumonia (CAP), defined by the need for intensive care unit (ICU) admission [1,2], ranges from 6.6% to 16.7% [3–7]. Its mortality is high, with pneumonia/influenza being the eighth leading cause of death in the USA [8].

2007 Guidelines for the management of patients with CAP published by the American Thoracic Society (ATS) and the Infectious Diseases Society of America (IDSA) [1], suggest the use of severity of illness scores such as the Pneumonia Severity Index (PSI) [9] and CURB-65 [10] in addition to clinical judgement to help physicians to decide the most appropriate site of care. Both scores have been validated at the emergency department and were designed to predict 30 day-mortality. They mainly identify patients with a low risk of mortality that can be safely managed in an outpatient setting. In 2009, Rello developed a severity assessment score

for CAP patients based on the PIRO concept [11]. This PIRO-CAP score performed well as a 28-day mortality prediction tool in CAP patients requiring ICU admission, with a better performance than either the Acute Physiology and Chronic Health Evaluation (APACHE) II score [12] or the ATS/IDSA criteria [1] in this subset of patients.

Primary viral pneumonia is recognized as the most common and also the most severe pulmonary manifestation of 2009 Influenza A (H1N1) because it is associated with high morbidity and mortality. The increased prevalence of this condition may necessitate the use of triage in order to prioritize ICU resources; however, the accuracy of the available severity of illness scores in this condition is unknown. Our objective was to assess which scoring system was best able to predict ICU mortality in patients admitted to the ICU due to 2009 Influenza A (H1N1) infection. A secondary aim was to identify variables associated with poor outcome in the subset of patients with an estimated risk of death below 3.6%.

Methods

This was a prospective, international, multicentre, observational study in patients with severe CAP due to the 2009 Influenza A (H1N1) virus admitted to ICUs of 33 countries. Data were prospectively collected through a web-based eCRF: the European Society of Intensive Care Medicine Influenza A (H1N1)v Registry. Ethical approval was sought and obtained prior to any patients being entered into the registry. The need for informed consent was waived due to the observational nature of the study. There were 394 patients, of whom we excluded 77 due to unavailability of data to calculate the three pneumonia-specific scores or unknown outcome at ICU discharge. Patients (n = 52) who presented with acute exacerbations of asthma or chronic obstructive pulmonary disease (COPD) were also excluded from this analysis (Fig. 1).

CAP due to the 2009 Influenza A (H1N1) virus was defined as a patient fulfilling ATS/IDSA criteria for CAP [1] and having a positive respiratory sample for the virus by reverse transcriptase polymerase chain reaction or viral culture. Primary viral pneumonia was defined in patients presenting during the acute phase of influenza virus illness with ARDS and unequivocal alveolar opacification with negative respiratory and blood bacterial cultures.

Data were collected to describe the severity of illness of each patient on admission to ICU. These data included baseline descriptors of demographics, co-morbid conditions and also physiological status and organ supports. The simplified acute physiology score (SAPS 3) [13] and the APACHE II score [12] were calculated according to the original descriptions.

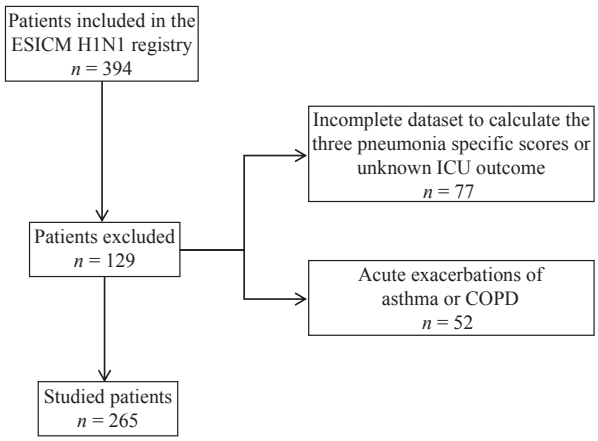

FIG. 1. Flowchart of enrolled patients.

Severity of CAP was evaluated using the PSI [9], CURB-65 [10] and PIRO-CAP [11] scores, which were calculated at the time of ICU admission. Patients were classified according to the original scores and were identified as having a low risk for mortality if the predicted mortality was between 0 and 3.6% [9–11]. This low risk of mortality corresponded to a PSI class of I, II or III, a CURB-65 score of 0 or 1, or a PIRO-CAP between 0 and 2. Patients with a PSI class ≥ IV, CURB-65 ≥ 3 or PIRO-CAP ≥ 4 were classified as high-risk patients.

Statistical analysis was performed using PASW 18.0 software (Chicago, IL, USA). The outcome variable of mortality was defined as all-cause mortality at the time of ICU discharge. Discrete variables are described as counts (%) and continuous variables as the mean with standard deviation (SD) or medians with 25th–75th interquartile range (IQR), as appropriate. Chi-square or Fisher's exact tests were used to compare categorical variables and Mann–Whitney *U*-tests for continuous variables. Receiver operating characteristic curves (ROC) were generated to compare the overall predictive accuracy of the scores for mortality, and the area under the ROC curves (aROC) was calculated. Variables associated with mortality were defined if a two-sided p value was ≤0.05; 95% confidence intervals were calculated. To determine factors potentially associated with ICU outcome, a multivariate logistic regression analysis was performed that included all significant variables from the univariate analysis, which were deemed clinically important before or at ICU admission. The sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) for each score were calculated according to standard criteria.

Results

Two hundred and sixty-five patients were enrolled in the study. These patients were from 31 different countries, from four continents. The main recruiting countries were: Portugal (55 cases), Spain (39 cases), Italy (39 cases), the UK (19 cases) and Argentina (18 cases). Patients were admitted to the hospital and to the ICU 5 (±4.66) and 7 (±5.87) days, respectively, after the onset of the symptoms.

The patients were 54% male with a mean age of 42 years (±16.1) and had an ICU admission SAPS 3 score of 54 (±15.9) and an APACHE II score of 22 (±8.7). No co-morbidity was present in 69 (26%) patients and 86 (33%) had associated bacterial pneumonia. Median ICU length of stay was 12 days (IQR, 6–22 days) and 84 (31.7%) patients died whilst in the ICU. Characteristics of the study population according to ICU outcome are shown in Table 1.

The number of patients and deaths in each class/score according to PSI, CURB-65 and PIRO-CAP with their actual and predicted mortality rates are shown in Table 2.

The mean PSI score was 103.2 ± 43.2 points, and was significantly related to ICU survival (survivors 92.6 ± 41.1 vs. non-survivors 126.1 ± 38.9; p <0.001). The relationship between the increase in the PSI class and the corresponding increase in ICU mortality was smooth (class I and II, 8.6% ICU mortality; class III, 22%; class IV, 38%; class V, 52%; p <0.001). The predictive accuracy of the PSI score, as evaluated by the aROC, was reasonable: 0.73 (95% CI, 0.67–0.78).

The mean CURB-65 in this group of patients was 1.7 ± 1.1 points and it was also significantly related to ICU survival (survivors 1.5 ± 1.1 vs. non-survivors 2.2 ± 1.1; p <0.001). Although there was a smooth relationship between an increasing score and ICU mortality (0 points, 13.9% ICU mortality; 1 point, 22.1%; 2 points, 33.3%; 3 points, 45.9%; ≥4 points, 66.7%; p <0.001), the accuracy, as evaluated by the aROC, was only 0.67 (95% CI, 0.59–0.74).

The PIRO-CAP score was on average 3.2 ± 1.5 points and it was significantly lower in ICU survivors (2.9 ± 1.5 vs. 3.7 ± 1.3; p <0.001). As in the other scores, the relationship between the increase in the score and the corresponding increase in ICU mortality was smooth (0–2 points, 13.7%

TABLE 1. Characteristics of study population split up by intensive care outcome

	Whole population (*n* = 265)	Survivor (*n* = 181)	Non-survivor (*n* = 84)	p
Age	42 ± 16.1	41 ± 15.8	45 ± 16.5	0.068
Gender, male (%)	142 (54)	96 (53)	46 (55)	0.794
SAPS 3 score	54 ± 15.9	51 ± 13.9	60 ± 18.2	<0.001
APACHE II score	22 ± 8.7	20 ± 8.0	25 ± 8.9	<0.001
Co-morbidities (%)	196 (74)	132 (72.9)	64 (76.2)	0.573
Diabetes mellitus	34 (12.8)	24 (13.3)	10 (11.9)	0.759
Asthma	11 (4.2)	7 (3.9)	4 (4.8)	0.747
COPD	14 (5.3)	10 (5.6)	4 (4.8)	1.0
Other chronic pulmonary disease	13 (4.9)	6 (3.3)	7 (8.3)	0.122
Cerebrovascular disease	7 (2.6)	4 (2.2)	3 (3.6)	0.682
Smoker	73 (27.7)	54 (30)	19 (22.6)	0.212
Arterial hypertension	64 (24.2)	45 (24.9)	19 (22.6)	0.691
Haematological neoplasia	24 (9.1)	13 (7.2)	11 (13.2)	0.119
Chronic hepatic disease	6 (2.3)	3 (1.7)	3 (3.6)	0.385
Autoimmune disease	7 (2.6)	5 (2.8)	2 (2.4)	1.0
Immunosuppression	3 (5.7)	2 (6.3)	1 (4.8)	1.0
Chronic renal failure	14 (5.3)	10 (5.5)	4 (4.8)	1.0
Corticotherapy	25 (9.5)	16 (8.9)	9 (10.7)	0.637
Chemotherapy	14 (5.3)	6 (3.3)	8 (9.5)	0.072
Pregnancy	16 (6)	13 (7.2)	3 (3.6)	0.251
Post-partum	6 (2.3)	6 (3.3)	0 (0)	0.181
Alcohol abuse	15 (5.7)	12 (6.6)	3 (3.6)	0.401
Congestive heart failure	9 (3.4)	5 (2.8)	4 (4.8)	0.471
Obesity (BMI > 30 kg/m^2)	24 (9.1)	14 (7.7)	10 (11.9)	0.271
Time from onset of symptoms to				
Hospital admission (days)	5 ± 4.7	4.8 ± 4.3	5.6 ± 5.4	0.234
ICU admission (days)	6.8 ± 5.9	6.6 ± 5.6	7.3 ± 6.3	0.352
Mechanical ventilation, days	12 (8–20)	12 (7–21)	13 (8–18)	0.736
ICU length of stay, days (median)	12 (6–22)	12 (5–22)	12 (7–23)	0.503
Associated clinical conditions (%)				
Bacterial pneumonia (*n* = 261)	86 (33)	60 (33.9)	26 (31)	0.636
Other infection (*n* = 260)	11 (4.2)	6 (3.4)	5 (6.0)	0.341
Septic shock (*n* = 261)	121 (46.4)	66 (37.3)	55 (65.5)	<0.001
Acute coronary syndrome (*n* = 261)	5 (1.9)	3 (1.7)	2 (2.4)	0.658
Acute renal failure (*n* = 261)	49 (18.8)	29 (16.4)	20 (23.8)	0.151
Acute consciousness change (*n* = 261)	80 (30.7)	42 (23.7)	38 (45.2)	<0.001
Rhabdomyolysis (*n* = 260)	41 (15.8)	20 (11.4)	21 (25)	0.005
Ventilatory strategies (%)				
Invasive mechanical ventilation (*n* = 263)	188 (75.3)	116 (64.8)	82 (97.6)	<0.001
Non-invasive ventilation (*n* = 260)	84 (32.3)	65 (36.7)	19 (22.7)	0.026

TABLE 2. Pneumonia severity scores

Score system	Global	Alive	Death	Predicted mortality (%)	p
PSI score (%)					
Class I and II	70 (26.4)	64 (91.4)	6 (8.6)	0.1/0.6	<0.001
Class III	41 (15.5)	32 (78)	9 (22)	0.9	
Class IV	79 (29.8)	49 (62)	30 (38)	9.5	
Class V	75 (28.3)	36 (48)	39 (52)	26.7	
CURB-65 score (%)					
0	36 (13.6)	31 (86.1)	5 (13.9)	1.5	<0.001
1	77 (29.1)	60 (77.9)	17 (22.1)	1.5	
2	93 (35.1)	62 (66.7)	31 (33.3)	9.2	
3	37 (14)	20 (54.1)	17 (45.9)	22	
4	21 (7.9)	7 (33.3)	14 (66.7)	22	
5	1 (0.4)	1 (100)	0 (0)	22	
PIRO-CAP score (%)					
Low risk (0–2)	73 (27.5)	63 (86.3)	10 (13.7)	3.6	0.001
Mild risk (3)	77 (29.1)	52 (67.5)	25 (32.5)	13	
High risk (4)	67 (25.3)	40 (59.7)	27 (40.3)	43	
Very high (≥5)	48 (18.1)	26 (54.2)	22 (45.8)	76.3	

TABLE 3. Severity scores according to presentation as either a primary viral pneumonia or as a bacterial co-infection

	Global		Only viral pneumonia		Bacterial co-infection	
Scores	aROC	95% CI	aROC	95% CI	aROC	95% CI
PSI	0.72	0.65–0.78	0.73	0.65–0.81	0.72	0.47–0.73
APACHE II	0.68	0.60–0.75	0.65	0.56–0.74	0.75	0.64–0.86
CURB-65	0.67	0.59–0.74	0.62	0.53–0.72	0.77	0.66–0.87
SAPS 3	0.66	0.58–0.73	0.70	0.62–0.79	0.57	0.42–0.71
PIRO-CAP	0.64	0.56–0.71	0.65	0.56–0.74	0.60	0.47–0.73

ICU mortality; 3 points, 32.5%; 4 points, 40.3%; ≥5 points, 45.8%; p 0.001) and the discriminatory power, as evaluated by the aROC, was only 0.64 (95% CI, 0.58–0.71).

The PSI score was the best predictor of mortality, with a reasonable discriminatory power (aROC, 0.73; 95% CI, 0.65–0.81) in patients with only primary viral pneumonia. On the other hand, CURB-65 showed the best accuracy (aROC, 0.77; 95% CI, 0.66–0.87) when bacterial co-infection was considered. The discriminatory power of PSI and PIRO-CAP was similar in patients with or without bacterial co-infection; however, in patients with bacterial co-infection the discriminatory power of CURB-65 and APACHE II significantly improved from 0.62 to 0.77 and from 0.65 to 0.75, respectively. On the opposite side, the accuracy of SAPS 3 decreased from 0.70 to 0.57 (Table 3).

In the overall population, a PIRO-CAP score ≥ 1 had the highest sensitivity (96.4%) whereas CURB-65 = 5 and PIRO-CAP 8 had the highest specificity (99.5%). All scores had low PPV, with CURB-65 ≥ 4 reaching the highest value (63.6%). The best NPV was associated with PSI ≥ 3 (91.4%) (Table 4).

The only variables independently associated with ICU mortality, by multivariate analysis, were the PSI score (OR 1.022 (1.009–1.034), p 0.001) and the need for mechanical ventilation at ICU admission (OR 20.629 (4.263–99.83), p <0.001).

Patients were classified at low risk of mortality according to the original scores. None of the scores were good at classifying this low-risk group. The PSI score identified 111 patients (41.9%) to be at a low risk of death, despite the fact that they had been admitted to and cared for in an ICU. This group had an ICU mortality of 13.5%. The CURB-65 score identified 113 patients as being at low risk with an observed mortality of 19.4%. Seventy-three patients were likewise categorized by the PIRO-CAP score and these had a mortality of 13.7%. Factors predicting death in these low-risk groups are described in Table 5.

Discussion

This study shows that severity scores underestimate ICU mortality in patients with 2009 Influenza A (H1N1) pneumonia. This information, comparing three different scores, is unique and adds value to the management of patients with CAP during the influenza season.

Although PSI presented the best ability to predict mortality, calibration was poor, with all scores underestimating ICU mortality (Fig. 2). PSI may underestimate severity, particularly

TABLE 4. Sensitivity, specificity, positive predicted value (PPV) and negative predictive value (NPV) for the evaluated scores

Score system	Sensitivity	Specificity	PPV	NPP
PSI				
≥Class III	92.9 (87.4–98.4)	35.4 (28.4–42.3)	40 (33.1–46.9)	91.4 (84.9–97.9)
≥Class IV	82.1 (73.9–90.3)	53 (45.8–60.3)	44.8 (36.9–52.7)	86.5 (80.1–92.8)
≥Class V	46.4 (35.8–57.1)	80.1 (74.3–85.9)	52 (40.7–63.3)	76.3 (70.3–82.4)
CURB-65				
≥1	94.1 (88.9–99.1)	17.1 (11.6–22.6)	34.5 (28.3–40.6)	86.1 (74.8–97.4)
≥2	73.8 (64.4–83.2)	50.3 (42.9–57.6)	40.8 (32.9–48.6)	80.5 (73.2–87.8)
≥3	36.9 (26.6–47.2)	84.5 (79.3–89.9)	52.5 (39.8–65.3)	74.3 (68.3–80.2)
≥4	16.7 (8.7–24.6)	95.6 (92.6–98.6)	63.6 (43.5–83.7)	71.2 (65.5–76.9)
≥5	0	99.4 (98.4–100)	0	68.2 (62.6–73.8)
PIRO-CAP				
≥1	96.4 (92.5–100)	7.2 (3.4–10.9)	32.5 (26.7–38.3)	81.2 (62.1–100)
≥2	94.0 (88.9–99.1)	17.1 (11.6–22.6)	34.5 (28.3–40.6)	86.1 (74.8–97.4)
≥3	88.1 (81.2–95.0)	34.8 (27.9–41.8)	38.5 (31.7–45.4)	86.3 (78.4–94.2)
≥4	58.3 (47.8–68.9)	63.5 (56.6–70.5)	42.6 (33.6–51.6)	76.7 (69.9–83.4)
≥5	26.2 (16.8–35.6)	85.6 (80.5–90.7)	45.8 (31.7–59.9)	71.4 (65.4–77.4)
≥6	4.8 (0.2–9.3)	97.8 (95.6–99.9)	50 (15.3–84.6)	68.9 (63.2–74.5)
≥7	1.2 (−1.1–3.5)	99.4 (98.4–100)	50 (−19–119)	68.4 (62.8–74.1)

TABLE 5. Risk factors for mortality in low-risk patients

		Univariate analysis			Multivariate analysis		
Severity score	**Variables**	**RR**	**95% CI**	**p**	**OR**	**95% CI**	**p**
PSI < 3	Other CPD	8.38	5.03–13.87	0.017	3.284	0.955–11.291	0.059
	Septic shock	2.6	1.02–6.42	0.05	3.221	1.861–5.576	<0.001
	Acute coronary syndrome	5.5	2.13–14.17	0.048	1.005	0.139–7.270	0.996
CURB 65 ≤ 1	Chemotherapy	3.4	1.50–7.77	0.05	7.393	1.629–33.552	0.01
	Bacterial pneumonia	0.1	0.02–0.89	0.007	0.787	0.429–1.443	0.439
	Rhabdomyolysis	2.8	1.34–5.72	0.017	2.248	1.090–4.638	0.028
	Invasive mechanical ventilation	11.7	1.68–83.54	<0.001	27.102	5.966–123.123	<0.001
PIRO CAP ≤ 2	Other CPD	5.8	2.08–16.38	0.048	2.467	0.725–8.393	0.148

RR, relative risk; OR, odds ratio; 95% CI, 95% confidence interval.

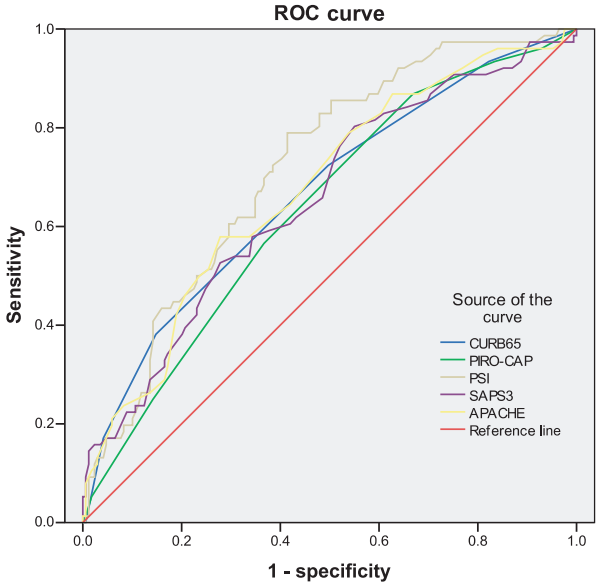

FIG. 2. Discriminatory power of severity scores (aROC).

in younger patients without co-morbidities who have severe respiratory failure. Similarly, CURB-65 may also underestimate risk in elderly patients with co-morbidities and in younger patients. As 2009 Influenza A (H1N1) infection occurred mainly in young patients with co-morbidities this may be one explanation for why these scores did not perform well. The second possible explanation is that severe respiratory failure was the main reason for ICU admission and all these scores underestimate this issue.

In patients with primary viral pneumonia, the discriminatory power of the different severity scores was reasonable and PSI was the best predictor of mortality with an acceptable discriminatory power (aROC 0.73). For patients with bacterial co-infection, the CURB-65 showed the best ability to predict ICU mortality. Neither of the general severity of illness scores was able to match the discrimination of the above two tools in these settings.

A scoring system with highest sensitivity is important in order not to miss the sickest patients and to minimize mortality. However, a very high sensitivity may also lead to a high burden of false-positive results. Our results showed that PIRO-CAP ≥ I had the highest sensitivity but PSI ≥ class III and CURB-65 ≥ 1 also showed a very good sensitivity. In the real world where ICU bed availability is a frequent problem, the PPV appears to become most important as it defines the proportion of patients severely ill who actually die. On this basis, a CURB-65 ≥ 4 was superior to the other studied scores yet none of them showed a significant result. Unlike PSI, CURB-65 ≥ 4 and PIRO-CAP ≥ 6 presented a very high specificity, 95.6% and 97.8%, respectively. In this study, PSI class ≥ 3 (92.8%) showed the highest NPV as compared with CURB-65 ≥ 1 (91.4%) and PIRO-CAP ≥ 3 (96.3%).

Our data discourage the use of these scores in patients with CAP due to 2009 Influenza A (H1N1) virus in order to decide site of treatment.

The accuracy of different pneumonia severity scores to predict ICU admission and hospital mortality in patients hospitalized for influenza was previously evaluated [14]. In this study, neither PSI nor CURB-65 was a good predictor of in-hospital mortality or ICU admission. Interestingly, their accuracy to predict in-hospital mortality evaluated by aROC was not quite different from their accuracy to predict ICU mortality in our study. Brandão-Neto *et al.* [15] suggested in an observational study of 53 patients hospitalized for pandemic 2009 Influenza A (H1N1) that PSI and CURB-65 perform poorly in this cohort of patients. In this study, these scores underestimate severity because, as in our study, a significant number of patients with low risk of mortality were admitted to the ICU. In fact, they observed that ICU admission occurred in 36.8% of the patients with a PSI score of I and II and in 49% of those with a CURB-65 score of 0–1. These results extend those of Mulrennan *et al.* [16] that the CURB-65 score, when applied to 2009 Influenza A (H1N1) was not suitable for predicting ICU admission. This is consistent with preliminary data regarding 2009 H1N1 influenza pneumonia [17].

SAPS3 and APACHE II scores were significantly higher in non-survivors than in survivors and this was also observed in

other case series [18–21]. However, their predictive accuracy was not significantly better than pneumonia-specific scores. In a study [22], APACHE II score showed a good accuracy (aROC 0.84) in predicting severity in 2009 Influenza A (H1N1). Yet, its application outside the ICU has not been validated and its application to all patients in the emergency department is complex.

All these scores do not perform well with regard to identification of patients with a low risk of death. In our low-risk group of patients, risk factors associated with higher mortality were severe respiratory failure (assumed to be the need for mechanical ventilation), other chronic pulmonary disease than COPD, chemotherapy and the presence of associated clinical conditions such as septic shock, acute coronary syndrome and rhabdomyolysis. Therefore, physicians should be cautious about the management of low-risk patients if at least one of the risk factors identified in this study is present. It is likely that these patients should be admitted to the hospital (eventually to the ICU) and carefully reassessed in order to decide on the best site of treatment. This is the first large study that has evaluated the accuracy of several specific severity scores in patients admitted to the ICU due to 2009 Influenza A (H1N1) infection. As with all observational studies, this study has several limitations. The PSI and CURB-65 were developed and validated to be used in the emergency department and not at ICU admission. Their use in patients already admitted to an ICU changes the sampling space of the score and may have introduced some discriminatory and calibration bias. This is an important problem, as it introduces a major difference to the scores developed to be used in patients already admitted to an ICU (e.g. the PIRO-CAP). Also, the volunteer nature of the registry may have introduced a degree of selection bias in the development of the database.

Conclusions

In conclusion, our results suggest that severity of illness scoring systems in ICU patients with CAP due to 2009 Influenza A (H1N1) should not be used as a triage tool, as demonstrated by a significant mortality rate even in patients considered to be not meeting criteria for hospital admission.

Authors' contributions

All authors have made substantial contribution to the conception and design of the study as well as the drafting, revising and final approval of the version to be published. JMP and RM performed statistical analysis.

Acknowledgements

The authors are grateful to all participating ICUs and clinicians who dedicated a significant portion of their time to help in the study. This study was partially presented at the 2010 European Society of Intensive Care Medicine Congress.

Transparency Declaration

The authors declare that they have no competing interests.

Appendix 1. ESICM H1N1 Registry Contributors

National coordinators: Spain (Alejandro Rodriguez), Portugal (Ricardo Matos), Italy (Maurizia Capuzzo), UK (Andrew Rhodes), Colombia (Mario Villabon), Argentina (Rosa Reina, Carina Balasini), Ecuador (Diego Barahona), Ireland (Brian Marsh), Brazil (Eliezer Silva), Norway (Haans Flaaten), Iceland (Gisli Sigurdsson), Czech Republic (Zykova Ivana, Vladimir Cerny), Germany (Michael Quintel, Tobias Welte), Peru (Manuel Mayorga), France (Georges Offenstadt, Bertrand Guidet, Jean-Daniel Chiche), Israel (Phillip Levin), Switzerland (Hans-Ulrich Rothen), Hong Kong (Charles Gomersall), Iran (Seyed Mohammadreza Hashemian), Greece (Constantine Katsanoulas, Heleni Mouloudi), India (Farhad Kapadia), Austria (Andreas Valentin), Sweden (Goran Hedenstierna), Denmark (Anders Perner), Chile (Guillermo Bugedo), Finland (Esko Ruokonen)

Spain

Jordi Rello, Antoni Soriano Arandes, Thiago Lisboa, Alejandro Rodriguez, Ignacio Martin-Loeches (Joan XXIII Universitary Hospital), Juan C. Montejo, Ramón Peñíscola (Hospital Universitario 12 De Octubre), Cecilia Hermosa, Federico Gordo (Hospital Del Henares), Jaime Latour (H General Universitario De Elche), Loreto Vidaur (Hospital Donostia), Manuel Alvarez-Gonzalez (Infanta Cristina), Luis Alvarez-Rocha (Complexo Hospitalario Universitario A Coruña), Ana De Pablo (Hospital Del Sureste), Cristina Ferri, Lopez De Arbina Martinez (Hospital Josep Trueta), Cortés Cânones (Complexo Hospitalario Ourense), Josu Insausti (Hospital De Navarra), Jose Cambronero (Hospital Universitario Príncipe De Asturias), Beatriz Galvan (H U La Paz), José Luna (Hospital De Tortosa Verge De La Cinta), Rafael Blancas (Hospital Del Tajo), Carmen Garcia (Infanta Elena Hospital), Rafael

Sierra (Puerta Del Mar University Hospital), Francisco Fernández Dorado (Centro Médico Delfos), Pablo Monedero (Clínica Universidad Navarra), Jose Llagunes (General Valencia), Pedro Cobo (Hospital Punta De Europa, Algeciras, Cádiz), Antonia Socias (Hospital Son Llàtzer), Rafael Leon-Lopez (Hospital Universitario Reina Sofia), Elisabeth Esteban (Hospital Sant Joan De Déu), Marquina Lacueva (San Jorge), Monica Magret (Sant Joan Reus), Frutos Del Nogal (Severo Ochoa).

Portugal

Alexandra Dinis (UCIP, Hospital Pediátrico, CH de Coimbra), Anabela Bártolo (UCI, CH do Alto Ave, Guimarães), Armindo Ramos (UCI, Hospitais Privados de Portugal, Cascais), Carlos Franca (SMI, CH de Lisboa Norte), Celso Estevens (UCI, Hospital de Faro), Cristina Granja (UCIM, Hospital Pedro Hispano, Matosinhos), Custódio Fidalgo (UCI, Hospital de Santarém), Eduardo Almeida (UCI, Hospital Garcia de Orta, Almada), Estevão Lafuente (UCI, CH Tâmega e Sousa, Penafiel), Fernando Rua (SCI, CH do Porto), Francisco Esteves (UCI, CH Trás-os-Montes e Alto Douro, Vila Real), José Clemente (UCI, Hospital Nossa Senhora do Rosário, Barreiro), José Júlio Nóbrega (SMI, CH do Funchal), José Manuel Pereira (UCIPG, Hospital S. João, Porto), José Pedro Moura (UCI, CH do Alto Minho, Viana Do Castelo), Luís Paulo Trindade E Silva (ULS, Hospital Sousa Martins, Guarda), Luís Telo (UCIR, CH de Lisboa Norte), Lurdes Santos (UCIDI, Hospital S. João, Porto), Maria José Pedrosa (UCI, Hospital de Santo André, Leiria), Maria Oliveira, Margarida Resende (Hospital de Curry Cabral, Lisboa), Nuno Catorze (UCIP, CH Médio Tejo, Abrantes), Paula Coutinho (UCI, CH de Coimbra), Rosa Ribeiro (UCI, CH de Setúbal), Rui Moreno, Isabel Miranda, Ricardo Matos (UCIP, CH de Lisboa Central), Teresa Cardoso (UCIP, CH do Porto), Vítor Branco (UCI, CH da Cova da Beira, Covilhã).

Italy

Giacomo Bellani (San Gerardo Hospital, University of Milan Bicocca), Ros Urbino (Ospedale Molinette Torino), Adriano Peris (Careggi Teaching Hospital), Alessandro Amatu (Fondazione IRCCS Policlinico San Matteo, Rianimazione), Giorgio Berlot (Cattainara (Trieste), Federico Capra Marzani (Fondazione IRCCS Policlinico S.Matteo), Ulisse Corbanese (Rianimazione – Ospedale S. Maria dei Battuti-Conegliano), Antonio David (A.O.U. Policlinico 'G. Martino' Messina), Paolo Chiarandini (AOU – S. Maria della Misericordia), Francesco Della Corte (ASO Maggiore Novara), Maria Luisa Caspani (Fondazione Ospedale Maggiore Policlinico, Mangiagalli E Regina Elena), Conio Alessandra (Ospedale Infantile Regina Margherita), Valerio Mangani (S.Giovanni Di Dio Hospital), Romano Tetamo (Arnas Civico), Andrea Wolfler (Children's Hospital Buzzi), Giuseppe Tappatà (Macerata), Vivaldi Nicoletta (ASO 'SS Antonio e Biagioe C.Arrigo' Alessandria), Maurizia Capuzzo (Azienda Ospedaliero-Universitaria di Ferrara), Guido Bertolini (GiViTI Coordinating Center), Lorella Pelagalli (National Cancer Institute Rome), Alexandre Molin (Ospedale San Martino), Massimo Girardis (Policlinico Di Modena), Giuseppe Gristin (S. Camillo Hospital – Rome).

United Kingdom

Rupert Pearse, Ammy Lam (Barts and the London NHS Trust), Andrew Rhodes (St George's Hospital), Ian Crabb (Gloucester), Rebecca Cusack (Southampton), Rhiannon Jackson (Frimley Park Hospital NHS Trust), Chithambaram Veerappan (The Royal Oldham Hospital, Oldham), Craig Whiteley, Tony Ware (Guy's and St Thomas' NHS Foundation Trust), Stephan Dr. Krueper (University Hospital of North Staffordshire NHS Trust), Caleb Mckinstry (Cheltenham Genera Hospital), Andrew Ferguson (Craigavon Area Hospital), Francesca Rubulotta (St Mary).

Colombia

Mario Villabon (Hospital De San Jose Bogota), Erick Valencia (Sagrado Corazon).

Argentina

Susana Gonzalez (Hospital Pirovano), Carina Balasini (San Martín La Plata), Victor Cevallos (Hospital Velez Sarsfield), Alan Zazu (Clínica De Especialidades), Jeronimo Nahuel Chaparro Fresco (HIGA Rossi), Gabriel Galindez (Hospital Alejandro Korn), Rosa Reina (Hospital San Martín), Cecilia Barrios (Sanatorio Franchin), Carlos Lovesio (Sanatorio Parque).

Ecuador

Diego Barahona, Boris Villamagua, Mario Cadena (Hospital Eugenio Espejo), Estuardo Salgado (Clínica La Merced), Marìa Fernanda García (Hospital Eugenio– Neumologia), Gustavo Paredes (Hospital Del Sur).

Ireland

Maria Donnelly (Adelaide And Meath Hospital Dublin), Brian Marsh (Mater Misericordiae University Hospital), Donall O'Croinin (Mercy University Hospital), John Bates (UCHG), Niall Kavanagh (St Luke's General Hospital), Brian O'Brien (Waterford Regional), Rob Plant (Cork University Hospital), Michael Scully (Our Lady of Lourdes), Rachel Farragher (Portiuncula Hospital).

Brazil

Louise Oliveira (Centro Hospitalar Unimed), Sergio Mataloun (UNISA – Hospital Geral Do Grajaú), Vicente Souza Dantas,

Luiz Simvoulidis (Hospital Pasteur), Péricles Duarte (Hosp. São Lucas-FAG), Cintia Grion (Hospital Universitário De Londrina), Almir Germano (Hospital Universitario De Maringa).

Norway
Jon Henrik Laake (Rikshospitalet Medical Centre), Elin Helset (Oslo University Hospital, 0Ulleval), Dagny Klausen (Haugesund Sjukehus Helse Fonna), Hans Flaatten (Haukeland University Hospital), Kari Bruheim (St Olavs Hospital).

Iceland
Bjarki Kristinsson (Landspitali), Sigurdur E Sigurdsson (FSA).

Czech Republic
Jan Hrubý (KARIM VFN), Radka Valkova (ICU Infection's Department, Masaryk's Hospital Usti Nad Labem), Robert Janda (Karlovy Vary), Ivana Zykova (Krajska Nemocnice Liberec).

Germany
Andrea Kernchen (University Hospital of Goettingen), Frank Bloos (University Hospital Jena), Simone Rosseau (Charité), Jens Krassler (Fachkrankenhaus Coswig Gmbh), Frank Fischer (Klinikum Forchheim).

Peru
Abel Arroyo-Sanchez (Hospital Victor Lazarte Echegaray), Alejandro Barrionuevo Poquet (Hospital Nacional Carlos Alberto Seguin Escobedo), Ivan Ramos Palomino (Clínica San Gabriel), Fabiola Rafael (HCFAP), Juan Salasfoch (Hospital Regional Docente).

France
Gregory Dubar (Foch), Jean-Marie Tonnelier (University Hospital of Brest), Saber Barbar (CHU Dijon), Murielle Dobrzynski (CHU Morvan), Alexandre Mignon (Hopital Cochin).

Israel
Daniel Jakobson (Barzilai MC), Moti Klein (Soroka Medical Center), Eran Segal (Assuta Medical Center), Yaron Barlavie (Rambam Hospital), Moshe Hersch (Shaare Zedek Medical Center).

Switzerland
Zule Sicardi Salomón (Astrid Lindgren Childerns Hospital), Hervé Zender (Hôpital Neuchâtelois – La Chaux-De-Fonds), Hans U. Rothen (Dept. of Intensive Care Medicine, Bern University Hospital).

Hong Kong
Charles Gomersall (Prince of Wales), Kenny Chan (Pamela Youde Nethersole Eastern Hospital), Tom Buckley (Princess Margaret Hospital).

Iran
Seyed Mohammadreza Hashemian (Nritld (Masih Daneshvari)).

Yugoslavia
Uros Batranovic (Institute for Pulmonary Diseases of Vojvodina), Ilons Schaffer (Hospital Health Center Kikinda), Jelena Sretkovic (KC Kragujevac).

Greece
Despoina Koulenti (Critical Care Department Attikon University Hospital, Athen), Eleni Mouloudi (Hippokrateion General Hospital Thessaloniki), Phyllis-Maria Clouva-Molyvdas (ICU Thriassio Hospital of Eleusis).

India
Mohan Gurjar (Sanjay Gandhi Post Graduate Institute of Medical Sciences), Deepak Vijayan (Kerala Institute of Medical Sciences).

Austria
Georg Hinterholzer (Kaiser Franz Josef Spital Vienna, 1. Med), Alexander Kulier (Medical University of Graz).

The Netherlands
Carin Verlaat (Universitary Medical Center Nijmegen), Dirk Ebel (Slingeland Ziekenhuis).

Sweden
Johan Persson (Lund University Hospital), Sten Walther (THIVA, US, Linköping), Per Petersen (Uddevalla).

Belgium
Walter Swinnen (Az Sint-Blasius), Vincent Collin (Cliniques De L'europe – Saint-Michel).

Denmark
Hanne Olsen (OUH, Svendborg Sygehus).

Bolivia
Patricio Gutierrez (Hospital Materno Infantil – Caja Nacional de Salud).

Bosnia and Herzegovina
Guillaume Thiery (Clinical Center University Sarajevo).

Chile
Guillermo Bugedo (Universidad Católica).

Finland
Heikki Laine (Central Hospital of Mikkeli).

Lithuania

Arvydas Rumba (Clinics of Kaunas University of Medicine).

Mauritius

Sundaresan Maiyalagan (Fortis Clinique Darne).

Qatar

Jose Clemente (Centro Hospitalar Barreiro Montijo).

Viet Nam

Thinh Bui (Trung Vuong Hospital).

References

1. Mandell LA, Wunderink RG, Anzueto A *et al.* Infectious Diseases Society of America/American Thoracic Society Consensus Guidelines on the management of community-acquired pneumonia in adults. *Clin Infect Dis* 2007; 44 (suppl 2): S27–S72.
2. Kamath AV, Myint PK. Recognising and managing severe community acquired pneumonia. *Br J Hosp Med* 2006; 26: 76–78.
3. Marrie TJ, Shariatzadeh MR. Community-acquired pneumonia requiring admission to an intensive care unit: a descriptive study. *Medicine (Baltimore)* 2007; 86: 103–111.
4. Bauer TT, Welte T, Ernen C *et al.* Cost analyses of community-acquired pneumonia from the hospital perspective. *Chest* 2005; 128: 2238–2246.
5. España PP, Capelastegui A, Gorordo I *et al.* Development and validation of a clinical prediction rule for severe community-acquired pneumonia. *Am J Respir Crit Care Med* 2006; 174: 1249–1256.
6. Ewig S, de Roux A, Bauer T *et al.* Validation of predictive rules and indices of severity for community acquired pneumonia. *Thorax* 2004; 59: 421–427.
7. Riley PD, Aronsky D, Dean NC. Validation of the 2001 American Thoracic Society criteria for severe community-acquired pneumonia. *Crit Care Med* 2004; 32: 2398–2402.
8. National Center for Health Statistics. Health Statistics, 2006, http://www.cdc.gov/nchs/fastats
9. Fine MJ, Auble TE, Yealy DM *et al.* A prediction rule to identify low-risk patients with community-acquired pneumonia. *N Engl J Med* 1997; 336: 243–250.
10. Lim WS, van der Eerden MM, Laing R *et al.* Defining community acquired pneumonia severity on presentation to hospital: an international derivation and validation study. *Thorax* 2003; 58: 377–382.
11. Rello J, Rodriguez A, Lisboa T *et al.* PIRO score for community-acquired pneumonia: a new prediction rule for assessment of severity in intensive care unit patients with community-acquired pneumonia. *Crit Care Med* 2009; 37: 456–462.
12. Knaus WA, Draper EA, Wagner DP *et al.* APACHE II: a severity of disease classification system. *Crit Care Med* 1985; 13: 818–829.
13. Moreno RP, Metnitz PG, Almeida E *et al.* SAPS 3 – from evaluation of the patient to evaluation of the intensive care unit. Part 2: Development of a prognostic model for hospital mortality at ICU admission. *Intensive Care Med* 2005; 31: 1345–1355.
14. Muller MP, McGeer AJ, Hassan K, Marshall J, Christian M for the Toronto Invasive Bacterial Disease Network. Evaluation of pneumonia severity and acute physiology scores to predict ICU admission and mortality in patients hospitalized for Influenza. *PLoS One* 2010; 5: e9563.
15. Brandão-Neto RA, Goulart AC, Santana AN *et al.* The role of pneumonia scores in the emergency room in patients infected by 2009 H1N1 infection. *Eur J Emerg Med* 2011; [Epub ahead of print].
16. Mulrennan S, Tempone SS, Ling ITW *et al.* Pandemic Influenza (H1N1) 2009 pneumonia: CURB-65 score for predicting severity and nasopharyngeal sampling for diagnosis are unreliable. *PLoS One* 2010; 5: e12849.
17. Riquelme R, Jimenez P, Videla AJ *et al.* Predicting mortality in hospitalized patients with 2009 H1N1 influenza pneumonia. *Int J Tuberc Lung Dis* 2011; 15: 542–546.
18. Dominguez-Cherit G, Lapinsky S, Macias A *et al.* Critically ill patients with 2009 Influenza A (H1N1) in Mexico. *JAMA* 2009; 17: 1880–1887.
19. Kumar A, Zarychanski R, Pinto R *et al.* Critically ill patients with 2009 Influenza A (H1N1) in Canada. *JAMA* 2009; 17: 1872–1879.
20. Ugarte S, Arancibia F, Soto R. Influenza A pandemics: clinical and organizational aspects: the experience of Chile. *Crit Care Med* 2010; 38: e133–e137.
21. Perez-Padilla R, de la Rosa-Zamboni D, Ponce de Leon S *et al.* Pneumonia and respiratory failure from swine-origin Influenza A (H1N1) in Mexico. *N Engl J Med* 2009; 361: 680–689.
22. Oh WS, Lee SJ, Lee CS *et al.* A prediction rule to identify severe cases among adult patients hospitalized with pandemic Influenza A (H1N1) 2009. *J Korean Med Sci* 2011; 26: 499–506.