Eur Respir J 2012; 40: 1201–1210
DOI: 10.1183/09031936.00187811

Severity assessment of healthcare-associated pneumonia and pneumonia in immunosuppression

Maria Carrabba*,#, Marina Zarantonello*, Paola Bonara#, Cinzia Hu#, Francesca Minonzio#, Ivan Cortinovis*, Silvano Milani* and Giovanna Fabio*,#

ABSTRACT: The study compares the ability of the PSI (pneumonia severity index), CURB-65 (confusion, urea >7 mol·L^{-1}, respiratory rate ⩾30 breaths·min^{-1}, blood pressure <90 mmHg systolic or ⩽60 mmHg diastolic, and age ⩾65 yrs), CURB and CRB-65 scales and the Severe Community-Acquired Pneumonia (SCAP) score to predict 30-day mortality in healthcare-associated pneumonia (HCAP) patients, and analyses differences in the demographics, aetiology and outcomes of community-acquired pneumonia (CAP), HCAP and pneumonia in immunocompromised patients.

629 consecutive patients admitted to a tertiary care university hospital were prospectively categorised as having CAP (n=322) or HCAP (n=307), and the HCAP patients were further subdivided into those who were immunocompromised (n=219) or immunocompetent (n=88).

The 30-day mortality rate was 9.0% in the CAP group and 24.1% in the HCAP group. In the HCAP group, the PSI and SCAP scores had similar prognostic power (area under the curve (AUC) of 0.68 and 0.67, respectively) and performed better than the CURB-65 score (AUC ⩽0.62). Among the immunocompetent HCAP patients, the PSI and CURB-65 scores were more sensitive than the others at every threshold, whereas SCAP was more specific than both of these. In the immunocompromised group, the PSI was highly sensitive but poorly specific at all thresholds.

Our results suggest that prognostic tools should be designed for subsets of HCAP patients.

KEYWORDS: Community-acquired pneumonia, immunocompromised patients, severity scores

In 2005, the term ''healthcare-associated pneumonia'' (HCAP) was introduced by the guidelines of the American Thoracic Society (ATS) and the Infectious Diseases Society of America (IDSA) concerning nosocomial pneumonia [1]. This new category was based on data showing that multidrug-resistant (MDR) pathogens, prevalent in nosocomial infections, could be found in subjects who had ongoing interactions with the healthcare system, despite their status as outpatients [2, 3]; the guidelines recommended intensively treating HCAP patients with a combination of broad-spectrum antimicrobial drugs active against MDR pathogens [1].

The 2005 ATS/IDSA guidelines also considered the increasing number of elderly and/or severely disabled patients resident in nursing homes, and patients who were significantly immunocompromised because of the disease and/or therapy and were more likely to experience MDR infections.

Recent observational studies have shown that between 17 and 38% of patients hospitalised for pneumonia have HCAP [4–7]. Despite the latest advances in antimicrobial therapy and improved supportive care, HCAP is a major cause of morbidity, and leads to mortality rates of about 20%, which is twice as high as those observed in patients with community-acquired pneumonia (CAP) [3–9]. HCAP patients are generally older, have more comorbidities and disabilities, and more closely resemble patients with hospital-acquired pneumonia (HAP) or ventilator-associated pneumonia (VAP) than CAP patients [3, 8, 10]. They therefore require adequate in-patient care and the appropriate allocation of resources to intensive care units (ICUs) in order to minimise morbidity and mortality.

A number of scoring systems have been developed to improve the clinical management of CAP patients and assure better resource allocation [11–13]. The two most widely studied are the 20-variable Pneumonia Severity Index (PSI) [14] and the five-variable CURB-65 (confusion, urea >7 mol·L^{-1}, respiratory rate ⩾30 breaths·min^{-1}, blood pressure <90 mmHg systolic or ⩽60 mmHg diastolic, and age ⩾65 yrs) score [15]. The eight-variable Severe

AFFILIATIONS
*Dept of Clinical Sciences and Community, Università degli Studi di Milano, and
#Dept of Internal Medicine, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy.

CORRESPONDENCE
M. Carrabba
Dept of Internal Medicine, Pad. Granelli
Università degli Studi di Milano
Fondazione IRCCS Ca' Granda
Ospedale Maggiore Policlinico
Via F. Sforza 35
20122 Milan
Italy
E-mail: maria.carrabba@unimi.it

Received:
Oct 27 2011
Accepted after revision:
Feb 14 2012
First published online:
March 09 2012

European Respiratory Journal
Print ISSN 0903-1936
Online ISSN 1399-3003

Community-Acquired Pneumonia (SCAP) score has recently been developed for patients with severe CAP [16, 17], and seems to be accurate for ICU admission.

There are no specific rules for assessing the severity and the prognosis of HCAP patients, and the performance of the CAP prognostic tools has only been evaluated in a few, mainly retrospective, studies [7, 18–20]. Furthermore, most of the prospective studies have investigated cohorts of HCAP patients residing in nursing homes or extended-care facilities, or previously hospitalised patients [9, 12, 21]. However, HCAP is a heterogeneous disease that may be more or less severe in different patient populations and in patients with different reasons for having contacted the healthcare system [22]. In particular, it is still debated whether pneumonia in immunocompromised patients can be considered a form of HCAP or is a different entity [23], and there are no published data concerning the use of severity scores in immunocompromised outpatients who are non-neutropenic or HIV-negative.

The aims of this prospective study were: to compare the performance of PSI, CURB, CURB-65, CRB-65 and SCAP scores in evaluating the severity of pneumonia and predicting 30-day mortality in hospitalised HCAP patients; to discuss any differences in the demographics, aetiology and outcomes of CAP and HCAP patients, and those belonging to the different HCAP subsets; and to explore the predictive power of the scoring systems in immunocompromised (IC) and non-IC HCAP patients.

METHODS

Study subjects

Between 2005 and 2010, 1,066 consecutive adults with pneumonia aged $\geqslant$18 yrs were admitted to the Internal Medicine Department of Fondazione IRCCS Ospedale Maggiore Policlinico, an acute-care tertiary university hospital in Milan, Italy. Of these, 629 were considered eligible for this prospective observational study. CAP and immunocompromise were defined on the basis of the criteria used in the Italian study of CAP management in internal medicine departments [24], in which the authors have been involved since 2002. The patients were classified as having HCAP if they had been hospitalised for $\geqslant$2 days during the 90 days preceding admission; if they resided in a skilled nursing facility or other institution; if they had been undergoing chronic dialysis; if they had received home or 1-day hospital infusion therapy within the preceding 30 days; if they had received home or hospital wound care or if a member of their family was affected by MDR pathogens [1].

Immunocompromise was defined as the presence of malignancy (active solid or haematological), immunological disorders or immunosuppressive therapy (*e.g.* cytotoxic chemotherapy, the use of >20 mg prednisone per day, or any other immunosuppressant in the previous 4 weeks), severe malnutrition or cachexia.

The exclusion criteria were VAP, HAP, suspected or known aspiration pneumonia, active tuberculosis infection, or fungal or cytomegalovirus pneumonia and HIV positivity. Approval from the local institutional review board (Ethical Committee of the Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy) and the patients' informed consent was obtained. In all cases, the decision to admit and the choice of therapy was entirely at the discretion of the attending physician.

Data collection and evaluation

A record was made of demographic variables, clinical findings upon presentation, comorbidities, pre-admission therapy, chest radiographic findings, laboratory parameters, microbiological studies, the need for invasive mechanical ventilation, complications, the length of hospital stay (LOS), in-hospital mortality, and outcome at discharge and 30 days after admission. 30-day all-cause mortality was assessed by reviewing the medical records and/or by telephone interview. The patients in whom 30-day mortality could not be ascertained were excluded.

Clinical prognostic models

The patients were stratified into 30-day mortality risk groups on the basis of the PSI, the CURB, CURB-65, CRB-65 scoring systems and the SCAP score, all of which were calculated using the set of prognostic indicators collected upon admission. The parameters for each prognostic tool were converted into dichotomous variables. In the case of the PSI, the patients were divided into low-, intermediate- and high-risk classes [14]; in the case of CURB, CURB-65 and CRB-65, they were stratified on the basis of the number of criteria met and divided into low-, intermediate- and high-risk classes [15]. The SCAP score upon admission was calculated *a posteriori* using prospectively recorded variables, and the patients were divided into low-, intermediate- and high-risk classes [16].

Statistical analysis

Descriptive statistics were computed resorting to the Statistical Package for Social Sciences, version 17 (SPSS, Chicago, IL, USA). Differences in the baseline characteristics between HCAP and CAP patients and, within the HCAP group, between IC and non-IC patients were tested with the Chi-squared test or unpaired t-test, as appropriate. Stepwise logistic regression was used to select the set of variables associated with 30-day mortality and to compute adjusted estimates of mortality in the CAP, HCAP IC and HCAP non-IC patients. Differences in survival between these groups were tested using the log-rank test. Survival was assessed using the Kaplan–Meier product limit estimates. The performance of each prognostic rule (in terms of sensitivity, specificity, and positive and negative likelihood ratio) was assessed for different cut-off points. Exact confidence limits of sensitivity and specificity were derived from binomial distribution. The receiver operating characteristic (ROC) curves for each prognostic score system were traced and the area under each ROC curve (AUC) were computed. The pairwise differences between the AUC of the five prognostic score systems were tested with a Wald test. SAS Proc Logistic (SAS/STAT User's guide version 9, SAS Institute Inc., Cary, NC, USA) was used to fit logistic regression models, to assess the performance of the prognostic score systems and to carry out ROC curve analysis. The two-tailed significance threshold was set at $p<0.05$ for all tests, with the exception of the pairwise comparisons between AUCs. In this case the threshold was set to $p<0.005$, in accordance with Bonferroni principle.

RESULTS

Patient characteristics and outcomes

Of the 629 enrolled patients, 307 (49%) were classified as having HCAP and 322 (51%) as having CAP. Table 1 shows the characteristics of the two groups.

34.2% of HCAP patients and 48.8% of CAP patients were >80 yrs of age ($p<0.001$), and consequently, in the HCAP

TABLE 1 Baseline characteristics

	HCAP patients	CAP patients	p-value
Subjects n	307	322	
Demographic data			
Age yrs	72.8 (26–98)	75.0 (18–102)	0.073
Age <65 yrs	74 (24.1)	67 (20.8)	0.340
Age ⩾80 yrs	105 (34.2)	157 (48.8)	<0.001
Males	187 (60.9)	164 (50.9)	0.013
Antibiotics before presentation	137 (45.1)	88 (27.7)	<0.001
Active alcohol abuse	9 (4.4)	13 (5.4)	0.666
Comorbidities			
Cerebrovascular disease	66 (21.5)	103 (32.0)	0.004
Cardiovascular disease	135 (44.0)	151 (46.9)	0.472
Chronic renal failure	89 (29.0)	75 (23.3)	0.122
COPD	42 (13.7)	83 (25.8)	<0.001
Diabetes	51 (16.6)	56 (17.4)	0.832
Chronic liver disease	44 (14.3)	35 (10.9)	0.229
Malignancy	213 (69.4)	13[#] (4.0)	<0.001
Two or more comorbidities	203 (66.1)	167 (51.9)	<0.001
Clinical parameters upon admission			
Altered mental status	78 (25.4)	92 (28.6)	0.419
Congestive heart failure	41 (13.4)	49 (15.2)	0.569
Acute renal failure	24 (9.0)	13 (4.9)	0.063
Temperature <35°C or ⩾40°C	6 (2.0)	6 (1.9)	1.000
Systolic blood pressure <90 mmHg[¶]	4 (1.3)	3 (0.9)	0.719
Systolic blood pressure <90 mmHg or diastolic ⩽60 mmHg[+]	96 (31.3)	61 (18.9)	<0.001
Pulse rate ⩾125 beats·min^{-1}	20 (6.5)	18 (5.6)	0.738
Respiratory rate ⩾30 breaths·min^{-1}	61 (19.9)	59 (18.3)	0.685
Laboratory findings upon admission			
Blood urea nitrogen >7 mmol·L^{-1}[+]	190 (61.9)	165 (51.2)	0.008
Blood urea nitrogen ⩾11 mmol·L^{-1}[¶]	96 (31.3)	69 (21.4)	0.006
Glucose ⩾250 mg·dL^{-1}	13 (4.2)	20 (6.2)	0.288
Sodium <130 mEq	26 (8.5)	11 (3.4)	0.010
Haematocrit <30%	88 (28.7)	10 (3.1)	<0.001
P_{O_2} <60 mmHg or S_{a,O_2} <90%	71 (23.1)	102 (31.7)	0.020
pH <7.35	5 (1.6)	18 (5.6)	0.010
WBC <4000 cells·μL^{-1}	58 (18.9)	4 (1.2)	<0.001
P_{O_2} <54 mmHg or $P_{a,O_2}/F_{I,O_2}$ <250	34 (11.1)	44 (13.7)	0.336
Radiographic findings upon admission			
Pleural effusion	84 (27.4)	109 (33.9)	0.084
Multilobar involvement	80 (26.1)	61 (18.9)	0.035
Outcome measures			
LOS days	15.1 (1–91)	13.1 (1–52)	0.004
30-day mortality	74 (24.1)	29 (9.0)	<0.001
In-hospital mortality[§]	62 (20.2)	26 (8.1)	<0.001
30-day mortality in those aged ⩾80 yrs	40 (38.9)	25 (15.9)	0.003
PSI score	126.7 (23–226)	105.1 (8–215)	<0.001

Data are presented as n (%) or mean (range), unless otherwise stated. HCAP: healthcare-associated pneumonia; CAP: community acquired pneumonia; COPD: chronic obstructive pulmonary disease; P_{O_2}: oxygen tension; S_{a,O_2}: arterial oxygen saturation; WBC: white blood cells; P_{a,O_2}: arterial oxygen tension; F_{I,O_2}: inspiratory oxygen fraction; LOS: length of hospital stay; PSI: Pneumonia Severity Index. [#]: *in situ* cancer; [¶]: PSI cut-off level; [+]: CURB scale cut-off level; [§]: also after 30 days.

group the prevalence of cerebrovascular diseases (21.5% *versus* 32.0%; p=0.004) and COPD (13.7% *versus* 25.8%) was lower. However, HCAP had more associated comorbidities than CAP (66.1% *versus* 51.9%; p<0.001) and were more often affected by malignancy (69.4% *versus* 4.0%; p<0.001). A greater rate of HCAP patients (45.1%) were given antibiotics prior to hospital admission compared to CAP patients (27.7%; p<0.001). On admission, radiography revealed pneumonia with multilobar involvement more often in HCAP (26.1%) than in CAP patients (18.9%; p=0.035). Malignancy in 13 CAP and eight non-IC

TABLE 2 Healthcare-acquired pneumonia (HCAP) patient backgrounds

All HCAP patients	Overall[#]
Subjects n	307
HCAP criteria	
Hospitalisation for ⩾2 days in previous 90 days	74 (24.7)
Day hospital access in previous 30 days for intravenous therapy	137 (45.8)
Nursing home residents	18 (5.9)
Home wound care or home infusion therapy	105 (34.2)
Chronic dialysis	0 (0)
IC HCAP patients[¶]	219 (71.3)
Chemotherapy and/or immunosuppressive therapy	113 (36.8)
Long-term steroids ⩾20 mg·day^{-1}	40 (15.7)
Malignancy	213 (69.4)
Haematogenous malignancy	170 (55.4)
Neutropenic (ANC <1500 cells·μL^{-1})	16 (7.2)[+]

Data are presented as n (%), unless otherwise stated. IC: immunocompromised; ANC: absolute neutrophil count. [#]: including overlapping cases; [¶]: all IC patients met at least one HCAP criterion; [+]: ANC 501–1000 cells·μL^{-1}: seven patients; ANC 1001–1500 cells·μL^{-1}: nine patients.

HCAP patients was attributable to *in situ* cancer (skin, prostate or uterus).

Most of the dichotomous laboratory variables included in the PSI, SCAP, CURB-65, CURB or CRB-65 scores were able to discriminate HCAP from CAP patients.

Mortality was 24.1% in the HCAP group and 9% in the CAP group. In-hospital mortality was similar to 30-day mortality.

The univariate odds for 30-day mortality was three times higher in the HCAP group (OR 3.21, 95% CI 2.020–5.096). After adjusting for PSI, the odds in the HCAP group remained higher (OR 5.56, 95% CI 2.02–15.26). At stepwise logistic regression, mortality was found to be associated with age ⩾80 yrs, multilobar involvement, blood urea nitrogen ⩾11 mmol·L^{-1}, sodium <130 mEq, pulse rate ⩾125 beats·min^{-1}, cerebrovascular disease, malignancy and pleural effusion and R-squared 16.1%; residual Chi-squared 13.1 (18 degrees of freedom), p=0.78. The odds ratio adjusted for these covariates (OR 4.65, 95% CI 1.22–17.75) was still significant. The HCAP patients had a longer LOS (p=0.004).

Patient characteristics and outcomes in the HCAP subsets

Table 2 shows the backgrounds of HCAP patients, many of whom satisfied more than one HCAP criterion: 24.7% had been hospitalised for ⩾2 days in the previous 90 days, 5.9% were nursing home residents, 45.8% received 1-day hospital intravenous medical therapy (chemotherapy or supportive care), and 34.2% underwent home wound care or home infusion therapy. Among the 137 patients with 1-day hospital access in the previous 30 days, 114 were affected by haematogenous malignancies, eight by solid malignancies and 15 by thalassaemia major or autoimmune diseases.

The majority (71.3%) were IC because of the disease and/or therapy, all of whom met at least one HCAP criterion, and none was classified as having CAP. As this was a discriminating parameter, the 219 IC patients were compared with the 88 non-IC patients. Admission from a nursing home accounted for 13.6% of the latter and 2.7% of the former (p=0.001). Malignancy in eight non-IC HCAP patients was attributable to *in situ* cancer. These patients were defined as HCAP because two had been hospitalised for ⩾2 days in the previous 90 days, three received 1-day hospital intravenous medical therapy and two underwent home wound care.

Table 3 shows comorbidities, and clinical and laboratory variables in the two HCAP subsets. The non-IC patients were older (mean age 77.8 *versus* 70.8 yrs; p<0.001), and included three times more ⩾80-yr-olds than the immunocompromised patients.

The univariate odds for 30-day mortality were similar in these two groups of patients (OR 0.93, 95% CI 0.52–1.65). Even after adjustment for the covariates selected by stepwise logistic regression, the odds ratio (OR 1.02, 95% CI 0.35–2.96) remained close to 1.

There were no differences in PSI score or LOS between the two groups.

Figure 1 shows the Kaplan–Meier plot of 30-day survival in the study cohort: the trend was similar in the IC and non-IC HCAP patients (p=0.713).

Microbiological studies

The microbiological studies were performed in 253 out of 322 CAP patients (78.6%) and in 266 out of 307 HCAP patients (86.6%). Positivity was obtained in 23.3% of CAP patients and 30.8% of HCAP patients. Table 4 shows the microbiological findings in the groups and subgroups. Data on *Enterococcus* species isolation have been included because enterococci are considered a rare cause of lung infections, except in the setting of impaired immunity. *Enterococcus faecalis* and *Enterococcus faecium* have emerged as multi-resistant nosocomial pathogens in IC, critically ill and elderly patients with comorbidities (stroke, hypertension and vascular disease).

Severity scores

As shown in figure 2, all five scoring systems showed the same trend of increasing mortality with worsening risk group. In all the risk classes of each score, mortality was higher in the HCAP group. In terms of distribution, CURB, CRB-65 and SCAP classified the largest proportion of patients as being at low risk, whereas the PSI and CURB-65 classified the lowest proportion as low risk. Among the HCAP patients, the PSI low-risk class had the lowest aggregate 30-day mortality than the low-risk classes of all of the other scores.

Comparison of severity scores performance

Figure 3 shows the ROC curves, AUCs and their differences for all scores in all of the groups and subgroups. All the prognostic scores performed better in CAP patients than in HCAP patients. In the overall HCAP group, the PSI seemed to predict mortality better than the three CURB scores, though differences were not significant; also SCAP appeared to perform slightly better than CURB curves. In the subset of non-IC HCAP patients, the performance of all prognostic scores was similar to that

TABLE 3 Baseline comparison of immunocompromised (IC) and non-IC healthcare-acquired pneumonia patients

	Non-IC	IC	p-value
Subjects n	88	219	
Demographic data			
Age yrs	77.8 (28–98)	70.8 (26–97)	<0.001
Age <65 yrs	15 (17.0)	59 (26.9)	0.077
Age ⩾80 yrs	55 (62.5)	50 (22.8)	<0.001
Males	45 (51.1)	142 (64.8)	0.029
Antibiotics before presentation	32 (37.2)	105 (48.2)	0.097
Comorbidities			
Cerebrovascular disease	46 (52.3)	20 (9.1)	<0.001
Cardiovascular disease	54 (61.4)	81 (37.0)	<0.001
Chronic renal failure	32 (36.4)	57 (26.0)	0.095
COPD	19 (21.6)	23 (10.5)	0.016
Diabetes	17 (19.3)	34 (15.5)	0.498
Chronic liver disease	13 (14.8)	31 (14.2)	0.859
Malignancy	8[§] (9.1)	205 (93.6)	<0.001
Two or more comorbidities	63 (71.6)	140 (63.9)	0.231
Clinical parameters upon admission			
Altered mental status	40 (45.5)	38 (17.4)	<0.001
Congestive heart failure	15 (17.0)	26 (11.9)	0.266
Acute renal failure	9 (13.4)	15 (7.5)	0.147
Temperature <35°C or ⩾40°C	2 (2.3)	4 (1.8)	1.000
Systolic blood pressure <90 mmHg[#]	2 (2.3)	2 (0.9)	0.324
Systolic blood pressure <90 mmHg or diastolic ⩽60 mmHg[¶]	23 (26.1)	73 (33.3)	0.276
Pulse rate ⩾125 beats·min^{-1}	10 (11.4)	10 (4.6)	0.040
Respiratory rate ⩾30 breaths·min^{-1}	16 (18.2)	45 (20.5)	0.752
Laboratory findings upon admission			
Blood urea nitrogen >7 mmol·L^{-1}[¶]	56 (63.6)	134 (61.2)	0.795
Blood urea nitrogen ⩾11 mmol·L^{-1}[#]	33 (37.5)	63 (28.8)	0.137
Glucose ⩾250 mg·dL^{-1}	5 (5.7)	8 (3.7)	0.531
Sodium <130 mEq	12 (13.6)	14 (6.4)	0.067
Haematocrit <30%	9 (10.2)	79 (36.1)	<0.001
P_{O_2} <60 mmHg or S_{a,O_2} <90%	19 (21.6)	52 (23.7)	0.765
pH <7.35	4 (4.5)	1 (0.5)	0.025
WBC <4000 cells·μL^{-1}	2 (2.3)	56 (25.6)	<0.001
P_{O_2} <54 mmHg or $P_{a,O_2}/F_{I,O_2}$ <250	9 (10.2)	25(11.4)	0.843
Radiographic findings upon admission			
Pleural effusion	19 (21.6)	65 (29.7)	0.160
Multilobar involvement	21 (23.9)	59 (26.9)	0.667
Outcome measures			
LOS days	13.7 (1–41)	15.7 (2–91)	0.111
30-day mortality	22 (25.0)	52 (23.7)	0.883
In-hospital mortality[+]	20 (22.7)	42 (19.2)	0.530
30-day mortality in patients aged ⩾80 yrs	22 (100)	18 (34.6)	<0.001
PSI score	122.9 (23–226)	128.2 (53–205)	0.269

Data are presented as n (%) or mean (range), unless otherwise stated. COPD: chronic obstructive pulmonary disease; P_{O_2}: oxygen tension; S_{a,O_2}: arterial oxygen saturation; WBC: white blood cells; P_{a,O_2}: arterial oxygen tension; F_{I,O_2}: inspiratory oxygen fraction; LOS: length of hospital stay; PSI: Pneumonia Severity Index. [#]: PSI cut-off level; [¶]: CURB scale cut-off level; [+]: after 30 days; [§]: *in situ* cancer.

observed in the CAP group. Among the IC HCAP patients, only the PSI and SCAP scores had prognostic value.

At every threshold, reported in table 5, the PSI was more sensitive and less specific than the CURB and SCAP scores, and also had the best negative likelihood ratio (0.19).

DISCUSSION

This prospective study analysed validated CAP scoring systems (PSI, CURB and its derivatives and SCAP) as predictors of 30-day mortality in hospitalised HCAP patients including immunocompromised patients; all scores are found to be poor at

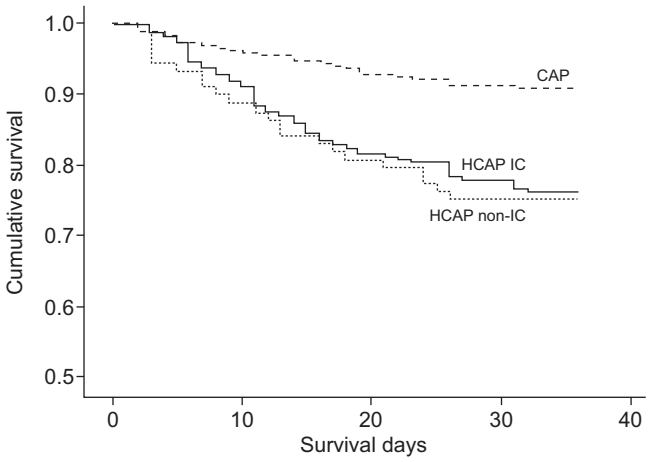


FIGURE 1. Kaplan–Meier plot of 30-day survival in healthcare-acquired pneumonia (HCAP) immunocompromised (IC), HCAP non-IC and community-acquired pneumonia (CAP) patients.

predicting 30-day mortality. The analysis of the two separate groups by immunocompetence showed that in HCAP patients without immunosuppression, all scores are good at predicting 30-day mortality and PSI is the best, while in HCAP patients with immunosuppression, all scores are poor at predicting 30-day mortality. The study also investigated the epidemiology of HCAP and the pneumonia of IC HCAP patients. Both the CAP and HCAP cohorts mainly consisted of elderly subjects with many chronic comorbidities. Cerebrovascular diseases and chronic obstructive pulmonary disease (COPD) were more prevalent in the CAP group. The most common pathogen in the CAP patients was *Streptococcus pneumoniae*, whereas the HCAP patients showed an increased incidence of pneumonia secondary to *Staphylococcus aureus* (methicillin-resistant *Staphylococcus aureus* and methicillin-sensitive *Staphylococcus aureus*), *Pseudomonas* spp. and other Gram-negative bacteria. The 30-day and in-hospital mortality rates in the HCAP group were 24.1% and 20.2%, respectively, as previously reported [3, 5, 7, 9]; the odds ratio for 30-day mortality with respect to CAP was 3.2.

The risk category distribution of our HCAP patients is the main difference between our study and previously published studies [3–7]. We did not enrol any patients undergoing haemodialysis or with aspiration pneumonia, and there was only a small proportion of nursing home residents, but there were many patients with cancer or who were IC as a result of therapy, thus making our HCAP cohort similar to that of PARK *et al*. [25], who reported a mean PSI of 104, with 29.7% of the patients in the low-risk class, and 10.4% in the high-risk CURB-65 class. However, their study was retrospective and there may have been some missing information.

TABLE 4 Distribution of isolated pathogens in community-acquired pneumonia (CAP) and immunocompromised (IC) and non-IC healthcare-acquired pneumonia (HCAP) patients

	Patients with indicated infections			
	CAP	HCAP	HCAP non-IC	HCAP IC
Pathogens				
Tested	253 (78.6)	266 (86.6)	68 (77.3)	198 (90.4)
Positive	59 (23.3)	82 (30.8)	22 (32.4)	60 (30.3)
Streptococcus pneumoniae	21 (35.6)	11 (13.4)	1 (4.5)	10 (16.7)
Staphylococcus aureus	4 (6.8)	13 (15.9)	5 (22.7)	8 (13.3)
MRSA	2 (3.4)	8 (9.8)	3 (13.6)	5 (8.3)
MSSA	2 (3.4)	5 (6.1)	2 (9.1)	3 (5.0)
Pseudomonas aeruginosa	5 (8.5)	9 (11.0)	4 (18.2)	5 (8.3)
***Enterococcus* spp.**	3 (5.1)	10 (12.2)	3 (13.6)	7[f] (11.7)
***Legionella* spp.**	5 (8.5)	4 (4.9)		4 (6.7)
Mycoplasma pneumoniae	2 (3.4)	4 (4.9)	2 (9.1)	2 (3.3)
Klebsiella pneumoniae	3 (5.1)	3 (3.7)		3 (5.0)
Chlamydia pneumoniae		1 (1.2)		1 (1.7)
Other Enterobacteriaceae[#]	2 (3.4)	3 (3.7)	2 (9.1)	4 (6.7)
Other non-fermenting Gram-negative rods[¶]	2 (3.4)	6 (7.3)	1 (4.5)	2 (3.3)
Coagulase-negative *Staphylococci*[+]	4 (6.8)	7 (8.5)	1 (4.5)	6 (10.0)
Escherichia coli	2 (3.4)	4 (4.9)	1 (4.5)	3 (5.0)
Haemophilus influenzae	1 (1.7)	3 (3.7)		3 (5.0)
Others[§]	3 (5.1)	6 (7.3)	3 (13.6)	3 (5.0)
Polymicrobial infection	6 (10.2)	9 (11.0)	3 (13.6)	6 (10.0)

Data are presented as n (%). MRSA: methicillin-resistant *Staphylococcus aureus*; MSSA: methicillin-sensitive *Staphylococcus aureus*. [#]: *Enterobacter* spp., *Citrobacter* spp., *Serratia marcescens*, *Proteus* spp. and *Morganella* spp.; [¶]: *Acinetobacter* spp., *Stenotrophomonas maltophilia*, *Pseudomonas fluorescens* and *Pseudomonas brevimundas*; [+]: *Staphylococcus haemolyticus*, *Staphylococcus hominis* and *Staphylococcus epidermidis*; [§]: *Brahamella* spp., *Corynebacterium* spp., *Streptococcus agalatiae*, *Streptococcus pyogenes*, influenza A H1N1 virus; [f]: two were vancomycin-resistant enterococci.

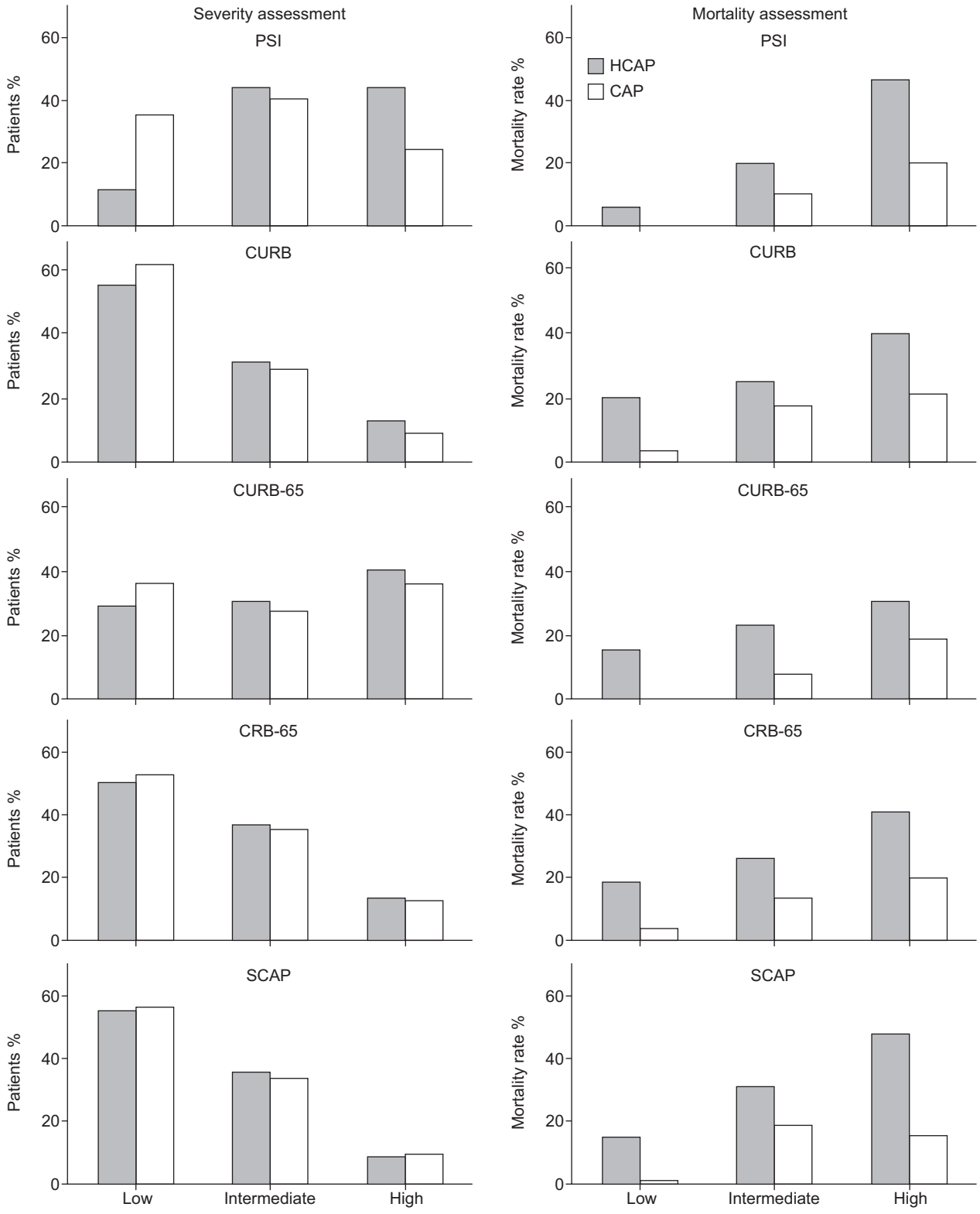
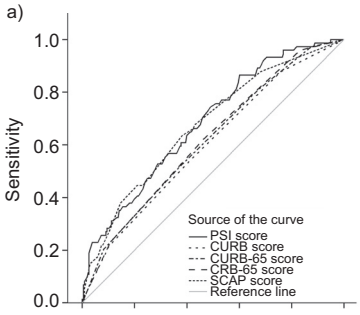


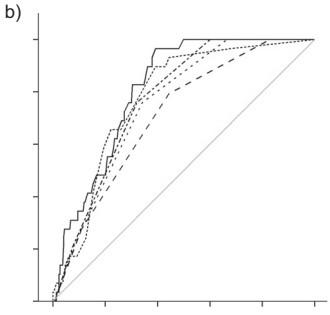
FIGURE 2. Severity assessment and 30-day mortality according to risk-classes. PSI: Pneumonia Severity Index; CURB: confusion, urea >7 mol·L^{-1}, respiratory rate ⩾30 breaths·min^{-1}, blood pressure <90 mmHg systolic or ⩽60 mmHg diastolic; CURB-65: confusion, urea >7 mol·L^{-1}, respiratory rate ⩾30 breaths·min^{-1}, blood pressure <90 mmHg systolic or ⩽60 mmHg diastolic, and age ⩾65 yrs; CRB-65: confusion, respiratory rate ⩾30 breaths·min^{-1}, blood pressure <90 mmHg systolic or ⩽60 mmHg diastolic, and age ⩾65 yrs; SCAP: severe community-acquired pneumonia score; HCAP: healthcare-acquired pneumonia; CAP: community-acquired pneumonia.



	AUC	95% CI	p-value
PSI score	0.68	0.62–0.75	<0.0001
CURB score	0.6	0.53–0.67	0.0027
CURB-65 score	0.62	0.55–0.69	0.0006
CRB-65 score	0.62	0.55–0.69	0.0003
SCAP score	0.67	0.6–0.74	<0.0001

Contrast	Difference	p-value
PSI *versus* CURB	0.08	0.0116
PSI *versus* CURB-65	0.07	0.0244
PSI *versus* CRB-65	0.06	0.0499
PSI *versus* SCAP	0.01	0.6972
CURB *versus* CURB-65	-0.01	0.1938
CURB *versus* CRB-65	-0.02	0.3466
CURB *versus* SCAP	-0.07	0.0084
CURB-65 *versus* CRB-65	0	0.7809
CURB-65 *versus* SCAP	-0.06	0.0389
CRB-65 *versus* SCAP	-0.05	0.063

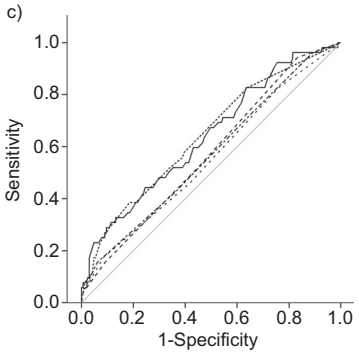
H_0: difference between areas = 0.
H_1: difference between areas ≠ 0.



	AUC	95% CI	p-value
PSI score	0.81	0.75–0.87	<0.0001
CURB score	0.75	0.69–0.82	<0.0001
CURB-65 score	0.77	0.71–0.83	<0.0001
CRB-65 score	0.71	0.63–0.79	<0.0001
SCAP score	0.78	0.7–0.85	<0.0001

Contrast	Difference	p-value
PSI *versus* CURB	0.06	0.0682
PSI *versus* CURB-65	0.04	0.1785
PSI *versus* CRB-65	0.1	0.0036
PSI *versus* SCAP	0.03	0.2738
CURB *versus* CURB-65	-0.02	0.0003
CURB *versus* CRB-65	0.04	0.0158
CURB *versus* SCAP	-0.02	0.5582
CURB-65 *versus* CRB-65	0.06	0.001
CURB-65 *versus* SCAP	-0.01	0.8797
CRB-65 *versus* SCAP	-0.07	0.0952

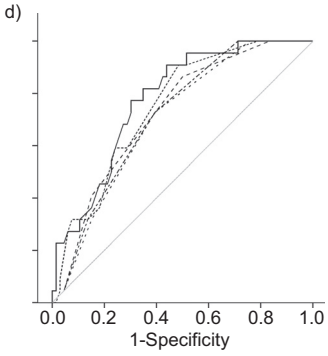
H_0: difference between areas = 0.
H_1: difference between areas ≠ 0.



	AUC	95% CI	p-value
PSI score	0.64	0.55–0.73	0.0009
CURB score	0.55	0.47–0.64	0.1158
CURB-65 score	0.57	0.48–0.65	0.0637
CRB-65 score	0.57	0.49–0.65	0.0428
SCAP score	0.64	0.56–0.73	0.0005

Contrast	Difference	p-value
PSI *versus* CURB	0.09	0.0354
PSI *versus* CURB-65	0.07	0.0485
PSI *versus* CRB-65	0.07	0.089
PSI *versus* SCAP	0	0.9113
CURB *versus* CURB-65	-0.01	0.3797
CURB *versus* CRB-65	-0.02	0.49
CURB *versus* SCAP	-0.09	0.0087
CURB-65 *versus* CRB-65	0	0.8256
CURB-65 *versus* SCAP	-0.08	0.0354
CRB-65 *versus* SCAP	-0.07	0.056

H_0: difference between areas = 0.
H_1: difference between areas ≠ 0.



	AUC	95% CI	p-value
PSI score	0.78	0.68–0.88	<0.0001
CURB score	0.7	0.6–0.81	0.0001
CURB-65 score	0.71	0.61–0.82	<0.0001
CRB-65 score	0.72	0.62–0.83	<0.0001
SCAP score	0.75	0.64–0.85	<0.0001

Contrast	Difference	p-value
PSI *versus* CURB	0.07	0.1786
PSI *versus* CURB-65	0.06	0.2419
PSI *versus* CRB-65	0.05	0.3412
PSI *versus* SCAP	0.03	0.4789
CURB *versus* CURB-65	-0.01	0.0743
CURB *versus* CRB-65	-0.02	0.4736
CURB *versus* SCAP	-0.05	0.349
CURB-65 *versus* CRB-65	-0.01	0.7376
CURB-65 *versus* SCAP	-0.03	0.4723
CRB-65 *versus* SCAP	-0.02	0.6001

H_0: difference between areas = 0.
H_1: difference between areas ≠ 0.

FIGURE 3. Receiver operating characteristics curves of scoring systems identifying patients at risk of death at 30 days in each patient group. Tables detail areas under the curves (AUC) and the comparison between scores. a) Healthcare-acquired pneumonia (HCAP) patients; b) community-acquired pneumonia patients; c) HCAP immunocompromised patients; d) HCAP non-immunocompromised patients. PSI: Pneumonia Severity Index; CURB: confusion, urea >7 mol·L^{-1}, respiratory rate ⩾30 breaths·min^{-1}, blood pressure <90 mmHg systolic or ⩽60 mmHg diastolic; CURB-65: confusion, urea >7 mol·L^{-1}, respiratory rate ⩾30 breaths·min^{-1}, blood pressure <90 mmHg systolic or ⩽60 mmHg diastolic, and age ⩾65 yrs; CRB-65: confusion, respiratory rate ⩾30 breaths·min^{-1}, blood pressure <90 mmHg systolic or ⩽60 mmHg diastolic, and age ⩾65 yrs; SCAP: severe community-acquired pneumonia.

The mean PSI of the HCAP patients in our study was 126.7, and 11.4% of them were in the low-risk class. However, the PSI and SCAP scores had opposite trends in both the CAP and HCAP groups: the smallest number was in the low-risk PSI class, and the highest number in the low-risk SCAP class. In our setting, PSI could be considered more useful than CURB-65 or SCAP in ruling out serious HCAP because of its high negative and low positive predictive values for 30-day mortality at all cut-off points, whereas SCAP is probably better suited to capture abnormal vital signs in acute illness as it includes multilobar radiographic infiltrates, hypoxia, acidosis and very old age. Nevertheless, its positive predictive value in the case of HCAP was as low as that of CURB and CRB-65, which may mean that none of them is useful in guiding decision-making for in-patients.

It has been argued that the HCAP population is highly heterogeneous, and that the HCAP concept may be misleading and creates confusion in the management of pneumonia [22]. However, we overcame this limitation by comparing our larger sub-group of IC HCAP patients with the sub-group of non-IC patients. Many HCAP studies [26] do not include IC patients and, although studies of IC patients have included HIV-positive subjects [5, 27, 28], there is a lack of data regarding the risks associated with pneumonia caused by drug-resistant pathogens in non-neutropenic cancer patients undergoing chemotherapy. Moreover, one study of neutropenic cancer patients found that no difference in risk was attributable to the type of malignancy, *i.e.* solid *versus* haematological malignancies [29].

The main differences between the two subgroups of IC and non-IC patients were age, cerebrovascular diseases and COPD: non-IC HCAP resembled CAP in terms of demographics and comorbidities. We did not observe any differences in admission parameters except for low haematocrit levels and leukopenia related to the underlying malignancy and/or therapy of IC patients. The two HCAP sub-groups also had similar 30-day and in-hospital mortality rates, and it is worth noting that both showed the same trend in 30-day survival. This suggests that very elderly patients with associated comorbidities and patients with advanced malignancies have a similarly high probability of dying during pneumonia.

Some authors have attempted to find a means of predicting the mortality risk in IC pneumonia patients, mainly those with HIV-infection or neutropenia [30, 31]. SANDERS *et al*. [32] retrospectively investigated the performance of PSI in IC HIV-negative patients, and found that ranking by mortality risk

TABLE 5 Sensitivity and specificity by patient group, risk class and prognostic scores

	Sensitivity	Specificity	PLR	NLR
HCAP				
PSI class				
⩾IV	0.973 (0.905–0.997)	0.142 (0.1–0.193)	1.13	0.19
⩾V	0.608 (0.488–0.720)	0.605 (0.539–0.668)	1.54	0.65
CURB score				
⩾2	0.541 (0.421–0.657)	0.588 (0.522–0.652)	1.31	0.78
⩾3	0.216 (0.129–0.327)	0.897 (0.851–0.933)	2.1	0.87
CURB-65 score				
⩾2	0.811 (0.703–0.893)	0.326 (0.266–0.390)	1.2	0.58
⩾3	0.514 (0.394–0.631)	0.631 (0.565–0.693)	1.39	0.77
CRB-65 score				
⩾2	0.622 (0.501–0.732)	0.536 (0.470–0.602)	1.34	0.71
⩾3	0.23 (0.140–0.342)	0.893 (0.846–0.929)	2.14	0.86
SCAP score				
⩾IV	0.459 (0.343–0.579)	0.729 (0.677–0.786)	1.70	0.74
⩾V	0.081 (0.030–0.168)	0.974 (0.945–0.990)	3.14	0.94
CAP				
PSI class				
⩾IV	1 (0.881–1)	0.389 (0.333–0.448)	1.64	0
⩾V	0.552 (0.357–0.736)	0.785 (0.733–0.831)	2.57	0.57
CURB score				
⩾2	0.759 (0.565–0.897)	0.659 (0.601–0.713)	2.2	0.37
⩾3	0.207 (0.080–0.397)	0.922 (0.885–0.950)	2.64	0.86
CURB-65 score				
⩾2	1 (0.881–1)	0.399 (0.343–0.458)	1.66	0
⩾3	0.759 (0.565–0.897)	0.679 (0.622–0.732)	2.36	0.36
CRB-65 score				
⩾2	0.793 (0.603–0.920)	0.556 (0.497–0.614)	1.79	0.37
⩾3	0.276 (0.127–0.472)	0.891 (0.849–0.924)	2.53	0.81
SCAP score				
⩾IV	0.621 (0.423–0.793)	0.778 (0.726–0.824)	2.80	0.49
⩾V	0.138 (0.039–0.317)	0.945 (0.913–0.968)	2.53	0.91
HCAP non-IC				
PSI class				
⩾IV	1.000 (0.846–1.000)	0.242 (0.145–0.364)	1.320	0.000
⩾V	0.773 (0.546–0.922)	0.652 (0.524–0.765)	2.217	0.349
CURB score				
⩾2	0.727 (0.498–0.893)	0.606 (0.478–0.724)	1.846	0.450
⩾3	0.318 (0.139–0.549)	0.848 (0.739–0.925)	2.100	0.804
CURB-65 score				
⩾2	1.000 (0.846–1.000)	0.288 (0.183–0.413)	1.404	0.000
⩾3	0.727 (0.498–0.893)	0.606 (0.478–0.724)	1.846	0.450
CRB-65 score				
⩾2	0.864 (0.651–0.971)	0.500 (0.374–0.626)	1.730	0.270
⩾3	0.409 (0.207–0.636)	0.848 (0.739–0.925)	2.700	0.700
SCAP score				
⩾IV	0.909 (0.708–0.989)	0.515 (0.389–0.640)	1.875	0.176
⩾V	0.318 (0.139–0.549)	0.894 (0.794–0.956)	3.000	0.763
HCAP IC				
PSI class				
⩾IV	0.962 (0.868–0.995)	0.102 (0.060–0.158)	1.071	0.378
⩾V	0.538 (0.395–0.678)	0.587 (0.508–0.662)	1.303	0.786
CURB score				
⩾2	0.462 (0.322–0.605)	0.581 (0.502–0.657)	1.101	0.927
⩾3	0.173 (0.082–0.303)	0.916 (0.863–0.953)	2.065	0.903
CURB-65 score				
⩾2	0.731 (0.590–0.844)	0.341 (0.270–0.419)	1.109	0.789
⩾3	0.423 (0.287–0.568)	0.641 (0.563–0.713)	1.178	0.900
CRB-65 score				
⩾2	0.519 (0.376–0.660)	0.551 (0.472–0.628)	1.156	0.873
⩾3	0.154 (0.069–0.281)	0.910 (0.856–0.949)	1.713	0.930
SCAP score				
⩾IV	0.519 (0.376–0.660)	0.659 (0.581–0.730)	1.521	0.730
⩾V	0.115 (0.044–0.234)	0.958 (0.916–0.983)	2.753	0.923

Data are presented as n (95% CI), unless otherwise stated. HCAP: healthcare-acquired pneumonia; IC: immunocompromised; PLR: positive likelihood ratio; NLR: negative likelihood ratio; CAP: community-acquired pneumonia; PSI: Pneumonia Severity Index; CURB: confusion, urea >7 mol·L^{-1}, respiratory rate ⩾30 breaths·min^{-1}, blood pressure <90 mmHg systolic or ⩽60 mmHg diastolic; CURB-65: confusion, urea >7 mol·L^{-1}, respiratory rate ⩾30 breaths·min^{-1}, blood pressure <90 mmHg systolic or ⩽60 mmHg diastolic, and age ⩾65 yrs; CRB-65: confusion, respiratory rate ⩾30 breaths·min^{-1}, blood pressure <90 mmHg systolic or ⩽60 mmHg diastolic, and age ⩾65 yrs; SCAP: severe community-acquired pneumonia scale.

reflected the groupings by different causes of immunological impairment. They pointed out that the PSI was an ''equally valid predictor of outcomes in the subset of patients not undergoing active cancer treatment''. We did not split our IC patients into sub-groups and found that the PSI was fairly good at predicting 30-day mortality.

However, further investigations are necessary to evaluate whether any other blood biomarker or parameter could be added to the 20 variables of the PSI in order to improve its performance in IC patients. The use of CURB and its derivatives to predict 30-day mortality in (particularly IC) HCAP patients is limited by its low prognostic accuracy.

Our data show that it may be useful to use SCAP scores in the clinical management of IC patients, in whom it seems to reflect acute pneumonia-related illness appropriately. SCAP was the most specific score in the highest risk class, and none of these patients survived.

Our study has a number of limitations: it involved only a single centre; younger patients with severe pneumonia admitted directly to ICUs from the emergency department were lost; and we were unable to determine the true impact of the patients' performance status on patient outcome. Furthermore, the large majority of the HCAP outpatients admitted because of pneumonia were affected by malignancies or were IC as a result of therapy.

The heterogeneity of the HCAP population is a major concern because it is known that the distribution and characteristics of HCAP depend on the local setting, which may affect the incidence of different causative organisms with different rates of antibiotic resistance [33]. Some authors have even claimed that IC patients should not be regarded as having HCAP, but various disease-specific characteristics should be considered when making treatment decisions [23, 34].

The strong points of our study seem to be the complete prospective data collection and the homogeneity of each of the HCAP subsets, some of which may have their own distinctive epidemiology and risk factors. In conclusion, while awaiting the development of an optimal predictive instrument, it seems that combining the information offered by different and complementary prognostic systems may be useful in different groups of HCAP patients.

SUPPORT STATEMENT

This study was supported by Ricerca Corrente funds, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy.

STATEMENT OF INTEREST

None declared.

ACKNOWLEDGEMENTS

Particular thanks to K. Smart (LINK, Milan, Italy) for his English review.

REFERENCES

1 American Thoracic Society, Infectious Diseases Society of America. Guidelines for the management of adults with hospital-acquired, ventilator-associated, and healthcare-associated pneumonia. *Am J Respir Crit Care Med* 2005; 171: 388–416.

2 Friedman ND, Kaye KS, Stout JE, *et al.* Healthcare-associated bloodstream infections in adults: a reason to change the accepted definition of community-acquired infections. *Ann Intern Med* 2002; 137: 791–797.
3 Kollef MH, Shorr A, Tabak YP, *et al.* Epidemiology and outcomes of health-care-associated pneumonia: results from a large US database of culture-positive pneumonia. *Chest* 2005; 128: 3854–3862.
4 Carratalà J, Mykietiuk A, Fernandez-Sabe N, *et al.* Healthcare-associated pneumonia requiring hospital admission: epidemiology, antibiotic therapy, and clinical outcomes. *Arch Intern Med* 2007; 167: 1393–1399.
5 Micek ST, Kollef KE, Reichley RM, *et al.* Healthcare-associated pneumonia and community-acquired pneumonia: a single-center experience. *Antimicrob Agents Chemother* 2007; 51: 3568–3573.
6 Venditti M, Falcone M, Corrao S, *et al.* Outcomes of patients hospitalized with community-acquired, health care-associated, and hospital-acquired pneumonia. *Ann Intern Med* 2009; 150: 19–26.
7 Shindo Y, Sato S, Maruyama E, *et al.* Health-care-associated pneumonia among hospitalized patients in a Japanese community hospital. *Chest* 2009; 135: 633–640.
8 Anand N, Kollef MH. The alphabet soup of pneumonia: CAP, HAP, HCAP, NHAP, and VAP. *Semin Respir Crit Care Med* 2009; 30: 3–9.
9 Rello J, Luján M, Gallego M, *et al.* Why mortality is increased in healthcare-associated pneumonia: lessons from pneumococcal bacteremic pneumonia. *Chest* 2010; 137: 1138–1144.
10 Muder RR, Aghababian RV, Loeb MB, *et al.* Nursing home-acquired pneumonia: an emergency department treatment algorithm. *Curr Med Res Opin* 2004; 20: 1309–1320.
11 Singanayagam A, Chalmers JD, Hill AT. Severity assessment in community-acquired pneumonia. *Q J Med* 2009; 102: 379–388.
12 Chalmers JD, Singanayagam A, Akram AR, *et al.* Severity assessment tools for predicting mortality in hospitalised patients with community-acquired pneumonia. Systematic review and meta-analysis. *Thorax* 2010; 65: 878–883.
13 Loke YK, Kwok CS, Niruban A, *et al.* Value of severity scales in predicting mortality from community-acquired pneumonia: systematic review and meta-analysis. *Thorax* 2010; 65: 878–883.
14 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.
15 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.
16 Espana 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.
17 Liapikou A, Ferrer M, Polverino E, *et al.* Severe community-acquired pneumonia: validation of the Infectious Diseases Society of America/American Thoracic Society guidelines to predict an intensive care unit admission. *Clin Infect Dis* 2009; 48: 377–385.
18 Kollef KE, Reichley RM, Micek ST, *et al.* The modified APACHE II score outperforms CURB65 pneumonia severity score as a predictor of thirty-day mortality on methicillin resistant *Staphylococcus aureus* pneumonia. *Chest* 2008; 133: 363–369.
19 Falcone M, Corrao S, Venditti M, *et al.* Performance of PSI, CURB-65, and SCAP scores in predicting the outcome of patients with community-acquired and healthcare-associated pneumonia. *Intern Emerg Med* 2011; 6: 431–436.
20 Fang WF, Yang KJ, Wu CL, *et al.* Application and comparison of scoring indices to predict outcomes in patients with health care associated pneumonia. *Crit Care* 2011; 15: R32.
21 El-Solh AA, Alhajhusain A, Jaoude PA, *et al.* Validity of severity scores in hospitalized patients with nursing home-acquired pneumonia. *Chest* 2010; 138: 1371–1376.
22 Brito V, Niederman MS. Healthcare-associated pneumonia is a heterogeneous disease, and all patients do not need the same broad-spectrum antibiotic therapy as complex nosocomial pneumonia. *Curr Opin Infect Dis* 2009; 22: 316–325.
23 Ewig S, Welte T, Chastre J, *et al.* Rethinking the concepts of community-acquired and health-care-associated pneumonia. *Lancet Infect Dis* 2010; 10: 279–287.
24 Blasi F, Iori I, Bulfoni A, *et al.* Can CAP guideline adherence improve patient outcome in internal medicine departments? *Eur Respir J* 2008; 32: 902–910.
25 Park HK, Song JU, Um SW, *et al.* Clinical characteristics of health care-associated pneumonia in a Korean teaching hospital. *Respir Med* 2010; 104: 1729–1735.
26 Attridge RT, Frei CR. Health care-associated pneumonia: an evidence-based review. *Am J Med* 2011; 124: 689–697.
27 Zilberberg MD, Shorr AF, Micek ST, *et al.* Antimicrobial therapy escalation and hospital mortality among patients with HCAP: a single center experience. *Chest* 2008; 134: 963–968.
28 Cecere LM, Rubenfeld GD, Park DR, *et al.* Long-term survival after hospitalization for community-acquired and healthcare-associated pneumonia. *Respiration* 2010; 79: 128–136.
29 Glasmacher A, von Lilienfeld-Toal M, Schulte S, *et al.* An evidence-based evaluation of important aspects of empirical antibiotic therapy in febrile neutropenic patients. *Clin Microbiol Infect* 2005; 11: 17–23.
30 Rano A, Agusti C, Benito N, *et al.* Prognostic factors of non-HIV immunocompromised patients with pulmonary infiltrates. *Chest* 2002; 122: 253–261.
31 Arozullah AM, Parada J, Bennett CL, *et al.* A rapid staging system for predicting mortality from HIV-associated community-acquired pneumonia. *Chest* 2003; 123: 1151–1160.
32 Sanders KM, Marras TK, Chan CK. Pneumonia severity index in the immunocompromised. *Can Respir J* 2006; 13: 89–93.
33 Kollef MH, Morrow LE, Baughman RP, *et al.* Healthcare-associated pneumonia (HCAP): a critical appraisal to improve identification, management, and outcomes. Proceedings of the HCAP Summit. *Clin Infect Dis* 2008; 46: S296–S334.
34 Yu VL. Guidelines for hospital-acquired pneumonia and health-care-associated pneumonia: a vulnerability, a pitfall, and a fatal flaw. *Lancet Infect Dis* 2011; 11: 248–252.