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Prognostic score systems and community-acquired bacteraemic pneumococcal pneumonia

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ABSTRACT: The aim of this study was to evaluate the accuracy of three score systems: the pneumonia severity index (PSI); CURB-65 (confusion; urea >7 mM; respiratory rate ⩾30 breaths·min^{-1}; blood pressure <90 mmHg systolic or ⩽60 mmHg diastolic; aged ⩾65 yrs old); and modified American Thoracic Society rule for predicting intensive care unit (ICU) need and mortality due to bacteraemic pneumococcal pneumonia.

All adult patients (n=114) with invasive pneumococcal pneumonia at the Karolinska University Hospital, Sweden, 1999–2000, were included in the study. Severity scores were calculated and the independent prognostic importance of different variables was analysed by multiple regression analyses.

PSI ⩾IV, CURB-65 ⩾2, and the presence of one major or more than one minor risk factor in mATS all had a high sensitivity, but somewhat lower specificity for predicting death and ICU need. The death rate was 12% (13 out of 114). Severity score and treatment in departments other than the Dept of Infectious Diseases were the only factors independently correlated to death. Patients treated in other departments more often had severe underlying illnesses and were more severely ill on admission. However, a significant difference in death rates remained after adjustment for severity between the two groups.

In conclusion, all score systems were useful for predicting the need for intensive care unit treatment and death due to bacteremic pneumococcal pneumonia. The pneumonia severity index was the most sensitive, but CURB-65 was easier to use.

KEYWORDS: Intensive care, pneumococcal bacteraemia, pneumococcal pneumonia, pneumonia, sepsis

Community-acquired pneumonia (CAP) remains a serious illness with a significant impact not only at an individual level, but also on society as a whole. In the USA, 0.5–1 million patients per yr are hospitalised for treatment of CAP [1]. Of these, ~10% require admission to an intensive care unit (ICU) [2]. The total case fatality rate for hospitalised patients is often 10–15% [3]. The costs of in-patient treatment are substantial and comprise the majority of the estimated $8.4 billion·yr^{-1} cost of treating CAP in the USA [4].

The potential severity of pneumonia and its economic impact have led to the development of a number of predictive score systems designed to optimise the care and treatment of CAP. The three most widely used predictive score systems for CAP are the pneumonia severity index (PSI), developed by FINE *et al.* [5] in 1997, the modified American Thoracic Society (mATS) rule (based on the ATS criteria for severe CAP) [6], and the most recently formulated severity score, CURB-65 (confusion; urea >7 mM; respiratory rate ⩾30 breaths·min^{-1}; blood pressure <90 mmHg systolic or ⩽60 mmHg diastolic; aged ⩾65 yrs old) [7].

These three severity scores have been developed for the very heterogeneous group of ''all'' CAP patients. PSI has been used to stratify for severity of illness in a recent study of monotherapy *versus* combination therapy for bacteraemic pneumococcal pneumonia [8]. Otherwise, these systems have not been evaluated for pneumonia caused by a single pathogen (*e.g.* pneumococcal pneumonia), except indirectly, since *Streptococcus pneumoniae* is the most common cause of CAP [9]. Positive blood cultures can be found in up to 20–30% of cases of pneumococcal pneumonia [10] and the incidence of bacteraemic disease in the community has been estimated as at least 10–20

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per 100,000 people per yr [11]. The mortality rate of bacteraemic pneumococcal pneumonia has remained at about the same level (~20%) in most studied areas since the introduction of antibiotic therapy, although lower figures (~10%) have been reported in some countries, *e.g.* Sweden [10, 12–14].

The aim of this study was to examine prospectively mortality in bacteraemic pneumococcal CAP and compare the accuracy of the PSI, CURB-65 and mATS systems for prediction of ICU treatment need and death.

MATERIALS AND METHODS

All adult patients (n=114) with community-acquired (no treatment in hospital within 30 days of the present admission) invasive pneumococcal disease (IPD) and radiography-verified pneumonia who were admitted to the Karolinska University Hospital, Solna, Sweden, between December 1998 and January 2001 were included in the study.

Most patients (n=86) were included prospectively on admission to the Dept of Infectious Diseases (DID), as a part of an international multicentre study on the effect of antibiotic resistance on the outcome of IPD [14]. The microbiological laboratory notified the current authors when a patient admitted to the DID had a blood culture positive for *S. pneumoniae*. This would usually take place within 24–48 h of admission to the hospital. Patients who fulfilled the inclusion criteria were included in the study. At the end of the prospective inclusion period, the present authors reviewed the records of the microbiological department for patients treated for IPD during the same period of time in other parts of the hospital. A total of 26 patients had been treated in other departments (OD). In addition, there were two patients who had been treated in DID but by mistake had not been included in the earlier study. These 28 patients were included retrospectively. Identical case record forms were used for both groups. Most of the information needed for calculation of the severity scores, both for prospectively and retrospectively included patients, was collected from medical records and laboratory databases, since these data had been collected and registered by the doctor and nurses in charge of the patient on admission.

The main reason why a patient with bacteraemic pneumococcal pneumonia is not admitted to DID is the presence of an underlying disease requiring close supervision in another unit, *e.g.* haematology or rheumatology. Severity of disease *per se* is not a parameter that decides which ward a patient with IPD is to be treated in.

The current study was approved by the local human investigations committee.

Severity scores

PSI, CURB-65 and mATS scores were, with one exception, calculated according to the original publications [5, 7, 15]. In the emergency room of the Karolinska University Hospital, serum creatinine, rather than serum urea, is the commonly used test of renal function. Serum creatinine has also been used as an alternative to urea as a predictor for severe disease [16], a procedure that was recommended in the 2001 ATS guidelines [17]. However, the cut-off values for serum urea used in PSI and CURB-65 are not the same (>10.7 mM and >7 mM, respectively). The current authors therefore chose to use a serum creatinine value of $\geqslant$130 mM, which corresponds to the higher of the two urea levels, for both scores. For calculating severity scores, all missing data were considered normal. There was no difference in the percentage of missing data between patients included prospectively or retrospectively (data not shown).

High-risk patients were defined as those having on admission a PSI risk class IV–V, a CURB-65 risk class 3–5, or mATS with >1 minor or $\geqslant$1 major criteria present. As a comparative baseline of severity, Acute Physiologic and Chronic Health Evaluation (APACHE)-II scores were also calculated [18]. The APACHE-II score is probably the best-established severity score overall, and although quite laborious to use, it has also been shown to correlate well with mortality in IPD [13, 14].

Statistics

Fisher's exact test or the unpaired t-test were used when appropriate. Multiple logistic regression models were used to analyse independent risk factors for the ICU treatment need and death.

RESULTS

The median age (range) of the 114 patients was 59 yrs (18–93) and there was a slight predominance of males. As can be seen in table 1, chronic heart disease and cancer were the most common comorbidities, and an underlying condition, including smoking, was present in 75% of cases. On admission, one-third of the patients had multilobar pneumonia, 13% were in septic shock and 18% required treatment in the ICU. The overall mortality was 11.4% (13 out of 114).

The APACHE-II score (categorised in 10-point strata) correlated directly with the need for ICU treatment. ICU treatment was necessary in 2% of patients with APACHE-II scores of 0–10, 14% of those with a score of 11–20, 75% with a score of 21–30, and 100% (three patients) of those with scores >30 (fig. 1). There was also a clear correlation between APACHE-II and the risk of death, and no patient with a score below 14 on admission died (fig. 2).

Pneumonia-specific severity scores

The need for ICU treatment was significantly higher ($p<0.0001$) in high-risk than in low-risk patients for all three severity scores: 19 out of 53 (35.8%) *versus* one out of 61 (1.6%) for PSI; 12 out of 22 (54.5%) *versus* eight out of 92 (8.7%) for CURB-65; and 18 out of 27 (66.7%) *versus* two out of 87 (2.3%) for mATS (fig. 1). Similarly, a significantly higher mortality ($p<0.01$) was seen in high-risk than in low-risk patients: 13 out of 53 (24.5%) *versus* 0 out of 61 for PSI; eight out of 22 (36.4%) *versus* five out of 92 (5.4%) for CURB-65; and 11 out of 27 (40.7%) *versus* two out of 87 (2.3%) for mATS (fig. 2).

As can be seen in figure 1, there was a gradual increase in the need for ICU treatment with increasing CURB-65 severity scores, similar to that seen with APACHE-II scores, while for PSI all patients but one in need of ICU treatment had a score $\geqslant$IV. Similarly, with two exceptions, ICU treatment was only needed, in patients with one major, or two or more minor, mATS criteria. As can be seen in figure 2, a similar pattern was seen for the correlation between severity score and mortality.

TABLE 1 Demographic data and case fatality rates for all patients with bacteraemic pneumococcal pneumonia

Patients n	114
Age yrs	57.1±17.5
Males	62 (54.4)
Any underlying condition, including smoking	86 (75.4)
Smoking	50 (43.9)
Alcoholism	13 (11.4)
***i.v.* drug use**	2 (1.8)
HIV	6 (5.3)
Chronic heart condition	27 (23.7)
Chronic lung condition	12 (8.4)
Chronic liver condition	2 (1.8)
Cancer	23 (20.2)
Immunosuppressive treatment	17 (14.9)
Diabetes mellitus	7 (6.1)
Cerebrovascular disease	5 (4.4)
Severity scores	
CURB-65 0	42 (36.8)
CURB-65 I	27 (23.7)
CURB-65 II	23 (20.2)
CURB-65 III	17 (14.9)
CURB-65 IV	4 (3.5)
CURB-65 V	1 (0.9)
PSI I–II	47 (41.2)
PSI III	14 (12.3)
PSI IV	31 (27.2)
PSI V	22 (19.3)
mATS 0	72 (63.2)
mATS 1 minor	15 (13.2)
mATS >1 minor and/or ⩾1 major	27 (23.7)
APACHE-II	12.8 (2–39)
ICU admission	20 (17.5)
Death	13 (11.4)

Data are presented as mean±SD, n (%) and mean (range), unless otherwise stated. CURB-65: confusion; urea >7 mM; respiratory rate ⩾30 breaths·min^{-1}; blood pressure <90 mmHg systolic or ⩽60 mmHg diastolic; aged ⩾65 yrs old; PSI: pneumonia severity index; mATS: modified American Thoracic Society rule; APACHE: Acute Physiologic and Chronic Health Evaluation; ICU: intensive care unit.

The only exception was for CURB-65 where the single patient in risk class 5 was treated in the ICU, but survived.

Sensitivity, specificity, positive and negative predictive values

All three scoring systems had a good accuracy for predicting a fatal outcome, with an area under the receiver operating characteristics curve between 0.83 and 0.87 (fig. 3). Using the high-risk definition, a cut-off for PSI of ⩾IV, for CURB-65 of ⩾3, and for mATS of >1 minor or ⩾1 major, the sensitivity/specificity of the three tests for predicting death were 100/60%, 62/86% and 85/84%, respectively (table 2). By lowering the cut-off for severe pneumonia for CURB-65 to ⩾2, the sensitivity and negative predictive values for this score increased to 92 and 99%, respectively, while the specificity and positive predictive value decreased to 67 and 27%, respectively.

Antibiotic treatment

The initial antibiotic treatments used were second- or third-generation cephalosporins (n=57 out of 114; 13 in combination with other antibiotics); a penicillin (mostly benzyl-penicillin) in monotherapy (n=42); carbapenems (n=6); fourth-generation cephalosporins (n=3); clindamycin (n=3); and n=1 each of piperacillin-tazobactam, ciprofloxacin and erythromycin. The 13 fatal cases were initially treated with: 1.5g cefuroxime three times·day^{-1} (n=8; one in combination with aminoglycoside); carbapenems (n=2); clindamycin (n=1); erythromycin (n=1; switched to clindamycin on day 2); and ciprofloxacin (n=1; switched to clindamycin on day 3).

Resistance

Most (77 %) of the pneumococcal strains were fully susceptible to all tested antibiotics. Resistance was most commonly found for trimethoprim-sulfamethoxazole (16%). Only 4.4% of the strains had decreased susceptibility to penicillin, with minimum inhibitory concentration (E-test) ranging 0.25–2.0 mg·L^{-1}. Macrolide resistance was seen in 7% of the strains.

Serotypes

A specific pneumococcal serotype could be determined in 109 out of 114 patients. The most common serotypes were types 1 (16%), 14 (13%), 9V (10%) and 4 (8%). Fatal cases were seen especially among patients infected with serotypes 3 (two deaths out of four infected), 6A (two out of five), and 19F (two out of seven).

Multivariate analysis of risk factors for death

For APACHE-II and each of the three pneumonia-specific severity scores studied (PSI, CURB-65 and mATS), a logistic regression analysis was performed, using the severity score as the continuous variable. The only two factors that turned out to be independently correlated to death in each analysis were the respective severity score and treatment in OD than DID. For APACHE-II the odds ratio (OR; 95% confidence interval (CI)) for a fatal outcome was 1.24 (1.07–1.44) for each incremental score point. The corresponding ORs per point were 1.05 (1.02–1.08) for PSI (score I–V); 2.9 (1.44–5.74) for CURB-65 (score 0–5); and 10.25 (2.72–38.66) for mATS (score 0, 1 minor or (>1 minor or ⩾1 major)).

In the logistic regression analyses for APACHE II, PSI, CURB-65 and mATS, the ORs (95% CI) for risk of death in those being treated in OD, as compared with DID, were 10.85 (1.81–64.94), 9.86 (1.50–64.87), 11.57 (2.17–61.58) and 14.87 (2.12–104.44), respectively.

Patients treated elsewhere than DID

A greater proportion of patients in OD, as compared with DID, had severe underlying conditions such as cancer (57.7 *versus* 9.1%; p<0.001) and immunosuppressive treatment (42.3 *versus* 6.8%; p<0.001), while other conditions such as chronic heart failure or lung disorders were equally distributed between the groups. According to the severity scores, patients treated in OD more frequently presented with a severe disease on admission, although the absolute number of patients with severe disease was 1.5–2 times as great in DID than in OD (table 3). There was also a greater tendency for patients in OD to have presented with septic shock (19 *versus* 11%; non-significant), and required treatment in the ICU (31% *versus*

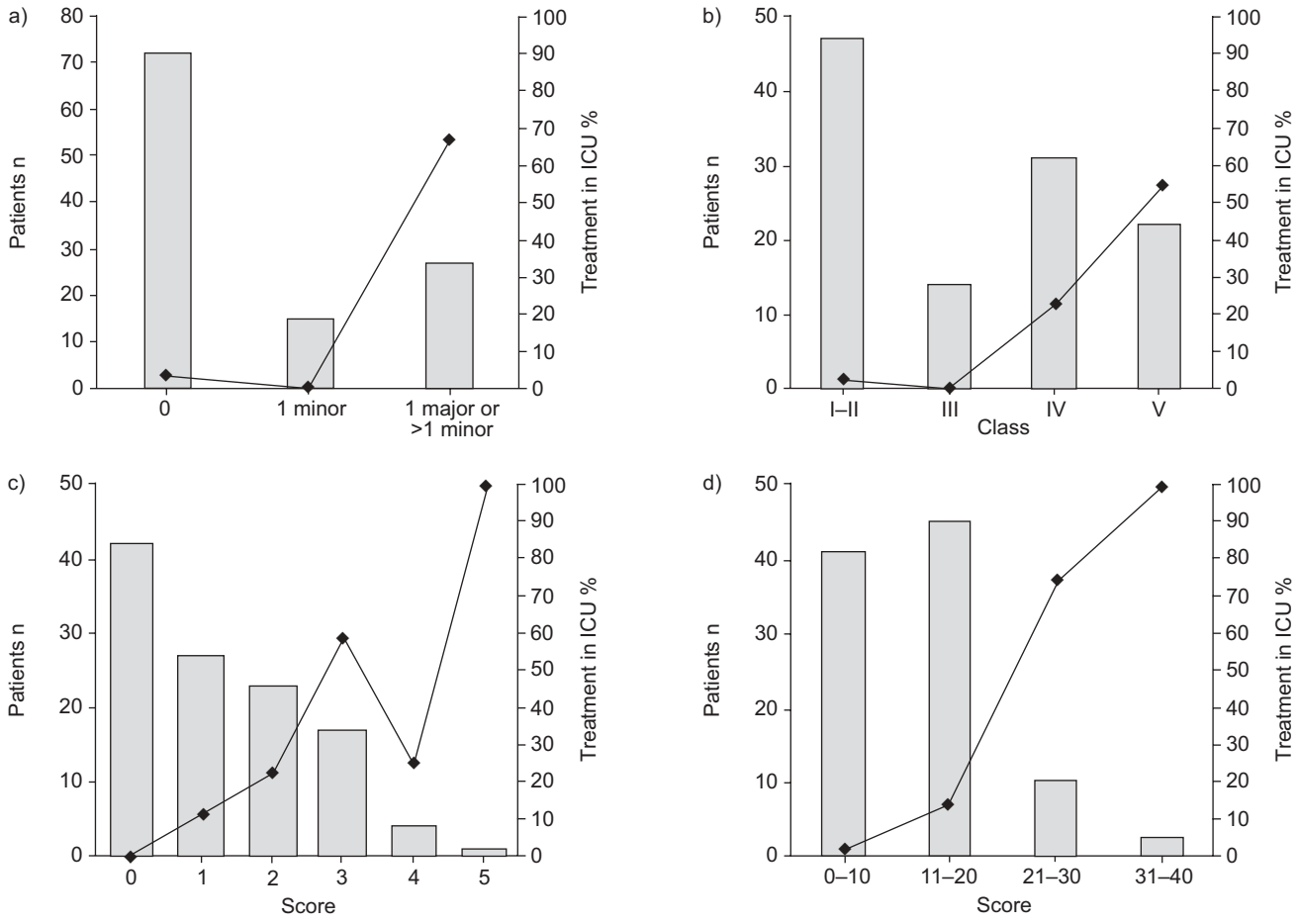

FIGURE 1. Intensive care unit admission rates within different score strata for a) modified American Thoracic Society rule; b) pneumonia severity index; c) CURB-65 (confusion; urea >7 mM; respiratory rate ⩾30 breaths·min^{-1}; blood pressure <90 mmHg systolic or ⩽60 mmHg diastolic; aged ⩾65 yrs old); and d) Acute Physiologic and Chronic Health Index-II score. ■: number of patients; ◆: intensive care unit admission.

14%; p=0.07), than those treated in DID. Serotype distribution also differed between the two groups, with serotypes 9V (19%), 6A (12%) and 19F (12%) being the most common in OD, compared with serotypes 1 (19%), 14 (15%) and 4 (9%) among patients treated in DID. No major differences between the two groups were seen in the antibiotic resistance pattern or in the empiric antibiotic treatment used. Unsurprisingly, patients treated in OD had a higher case-fatality rate than those treated in DID: 34.6 (nine out of 26) *versus* 4.5% (four out of 88; p<0.0001). However, this difference remained significant after stratification for severity (table 3). Among patients with the most severe disease (PSI IV–V, CURB-65 3–5 or mATS with >1 minor or ⩾1 major criterion), the case-fatality rates were about three times higher in patients treated in OD than in those treated in DID.

DISCUSSION

A severity-score system for CAP has to fulfil several criteria in order to work properly. It must have a high sensitivity and specificity, but it must also be easy to use; otherwise it is unlikely that the system will be of any practical use in the clinical setting. The current study population comprised patients with known bacteraemic pneumococcal pneumonia. On admission to hospital, this diagnosis may be suspected, but will often not be verified until 24–48 h later. However, since *S. pneumoniae* is the most common cause of fatal CAP [9], it is important to know whether the chosen prognostic score system will classify patients with pneumococcal pneumonia correctly.

In the current mixed prospective and retrospective study of bacteraemic pneumococcal CAP, three important observations were made. First, mortality from bacteraemic pneumococcal pneumonia remains on a low level (11%) in Stockholm, Sweden. Secondly, the pneumonia-specific severity-score systems PSI, CURB-65 and mATS, originally developed for CAP of ''unknown'' aetiology, are also useful for patients with bacteraemic pneumococcal pneumonia. Thirdly, despite adjustment for severity of disease, clinical outcome can differ considerably between patient groups, a fact which can probably be attributed to the fact that severe underlying diseases have low weight (PSI), or are not included at all (CURB-65 and mATS), in the calculation of the three scores.

Case-fatality in bacteraemic pneumococcal pneumonia

Earlier studies of bacteraemic pneumococcal pneumonia in Stockholm (1977–1995) have demonstrated similar case-fatality rates (7–11%) [13, 19] to that in the present study (11%; 13 out

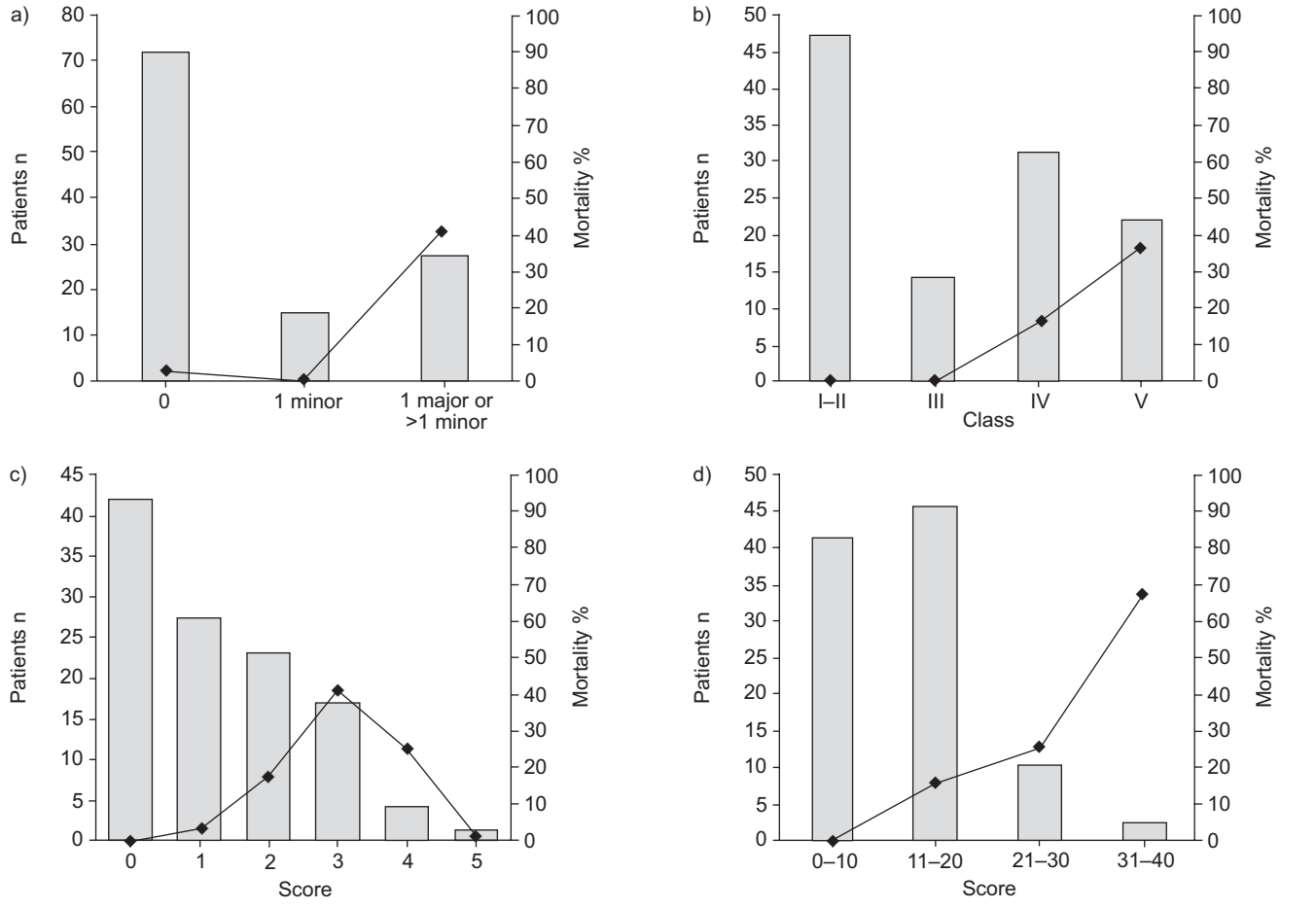

FIGURE 2. Case fatality rates within different score strata for a) modified American Thoracic Society rule; b) pneumonia severity index; c) CURB-65 (confusion; urea >7 mM; respiratory rate ⩾30 breaths·min^{-1}; blood pressure <90 mmHg systolic or ⩽60 mmHg diastolic; aged ⩾65 yrs old); and d) Acute Physiologic and Chronic Health Index-II score. ■: number of patients; ◆: mortality.

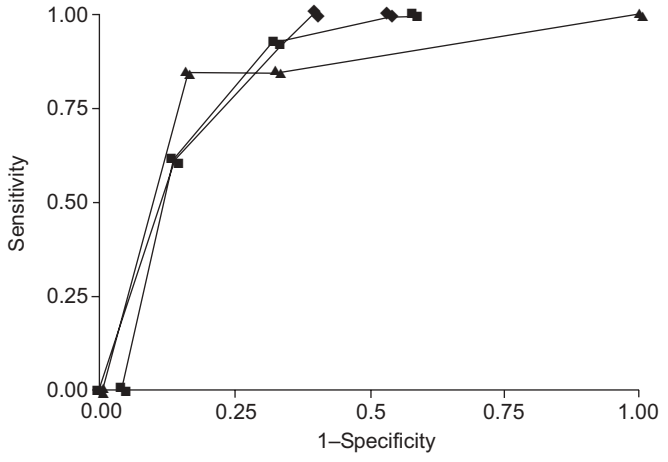

FIGURE 3. Receiver operating characteristic (ROC) curves for pneumonia severity index (PSI; ◆); modified American Thoracic Society (mATS; ▲) rule; and CURB-65 (confusion; urea >7 mM; respiratory rate ⩾30 breaths·min^{-1}; blood pressure <90 mmHg systolic or ⩽60 mmHg diastolic; aged ⩾65 yrs old; ■). Area under ROC curves: PSI 0.85; CURB-65 0.84; and mATS 0.83.

of 114). In contrast, case-fatality rates in studies of IPD from other centres, both inside and outside Sweden, have varied considerably, from ~3 to 25%, or higher [10, 14, 20–29]. These varying case-fatality rates are likely to be due to differences between study populations concerning demographics, underlying health characteristics or severity of illness on admission to hospital [12, 13]. Therefore, it must be of great importance to stratify patients according to severity of illness when comparing results between different sites. This strategy was applied in a recent in study where the Pitt bacteraemia score was used for defining patients who were critically ill (Pitt score >4) among 844 patients with invasive pneumococcal disease from 10 countries [14]. A Pitt score >4 had a predictive value for mortality of 81%, and was also shown to be highly correlated ($p=0.0001$) with the APACHE-II score.

Bacteraemic pneumococcal pneumonia and severity scores

In the present study, the APACHE-II score was used as a reference for the pneumonia-specific scores, since it has been shown to be highly correlated to the outcome of invasive pneumococcal disease [13, 14]. In the study by KALIN *et al.* [13], the case-fatality rate was only 2.6% in patients with an APACHE-II score <12 (the median value), compared with

TABLE 2 Sensitivity and specificity rates for the three tested score systems with regards to severe bacteraemic pneumococcal pneumonia

	Mortality			ICU treatment		
	PSI IV	CURB-65 3–5	mATS 1 major >1 minor	PSI IV–V	CURB-65 3–5	mATS 1 major/>1 minor
Sensitivity	100	62	85	95	71	90
Specificity	60	86	84	64	87	90
PPV	25	36	41	36	55	67
NPV	100	95	98	98	91	98

Data are presented as %. ICU: intensive care unit; PSI: pneumonia severity index; CURB-65: confusion; urea >7 mM; respiratory rate ⩾30 breaths·min^{-1}; blood pressure <90 mmHg systolic or ⩽60 mmHg diastolic; aged ⩾65 yrs old; mATS: modified American Thoracic Society rule; PPV: positive predictive value; NPV: negative predictive value.

21% for those with a score of ⩾12. This in accordance with the present study, in which no patient with an APACHE-II score <14 died, compared with 22% of those with a score ⩾14. Approximately the same ''cut-off level'' was found in two other studies, on bacteraemic pneumococcal pneumonia [26] and on severe all-cause pneumonia [30], respectively, which both demonstrated that an APACHE-II score >15 was associated with a poor outcome.

The pneumonia-specific severity scores were as effective as the APACHE-II score in identifying patients at high risk of death. The PSI, with a cut-off of ⩾IV, had the highest sensitivity and was the score that best identified patients with a low risk of death. Conversely, PSI had the lowest specificity: only 10% of patients with a score of ⩾IV actually died, compared with 40% of patients who had >1 minor or ⩾1 major criteria according to the mATS score. Furthermore, to calculate the PSI score, a large number of variables, including results of laboratory analyses and chest radiography, have to be provided, making this prognostic help difficult to implement in the routine clinical setting. (APACHE-II also suffers from this problem). The CURB-65 score has the obvious advantage of being very easy to use, requiring only five variables. With a cut-off ''high-risk'' score of ⩾2, CURB-65 performed similarly to PSI (cut-off ⩾IV), with a high sensitivity (92%) and a low specificity (67%). Conversely, a CURB-65 cut-off of ⩾3 resulted in a rather low sensitivity (62%) but a moderately good specificity (86%). mATS was the best system in terms of specificity and positive predictive value, and had only a slightly lower sensitivity. It should be taken into account that this is the only one of the tested score systems that is primarily aimed at finding the patients with the most severe pneumonia. However, the mATS rule can difficult to interpret in terms of ICU care, since the major criterion ''need for mechanical ventilation'' can only be obtained in an ICU at the Karolinska University Hospital, thus creating a circular argument.

TABLE 3 Differences in case-fatality rates (CFR) between patients treated for severe bacteraemic pneumococcal pneumonia in the department of infectious diseases (DID) and those treated in other departments (OD).

	PSI IV–V		CURB-65 3–5		mATS >1minor/⩾1 major	
	Patients	CFR	Patients	CFR	Patients	CFR
DID	33/88 (38)	4/33 (12)**	14/88 (16)$^{\#}$	3/14 (21)¶	18/88 (21)$^{\#}$	4/18 (22)**
OD	20/26 (77) ***	9/20 (45)**	8/26 (30)$^{\#}$	5/8 (63)¶	9/26 (35)$^{\#}$	7/9 (78)**

Data are presented as n/total (%). PSI: pneumonia severity index; CURB-65: confusion; urea >7 mM; respiratory rate ⩾30 breaths·min^{-1}; blood pressure <90 mmHg systolic or ⩽60 mmHg diastolic; aged ⩾65 yrs old; mATS: modified American Thoracic Society. **: DID *versus* OD, p<0.01; ***: DID *versus* OD, p<0.001; $^{\#}$: DID *versus* OD, nonsignificant; ¶: DID *versus* OD, p=0.08.

The case-fatality rate in the present study was much higher than in the derivation and validation cohorts of CURB-65 [7] (27 *versus* 16% for a cut-off of ⩾2; 36 *versus* 22–23% for a cut-off of ⩾3). Also, using PSI (scores of IV–V) or mATS scores, the patients in the present study with bacteraemic pneumococcal pneumonia had higher case-fatality rates than in studies of all-cause CAP [31–35]. One reason for this could be that invasive pneumococcal pneumonia is a more severe disease in itself than ''all-cause pneumonia''. Another possibility is that patients with invasive pneumococcal pneumonia more often have severe underlying conditions, but that these illnesses carry a low weight according to the severity scores. For CURB-65, there could have been a third reason, namely that the current authors used a cut-off value for S-creatinine that corresponded to a serum urea concentration of 11 mM instead of the 7 mM used in the original publication [7]. However, this made little difference to the case-fatality rate. If the lower serum urea level was applied, 28 instead of 22 patients would have had a ''high-risk'' pneumonia (score of ⩾3), with a case-fatality rate of 10 out of 28 (35.7%), as compared to eight out of 22 (36.4%) when the cut-off for serum urea concentration was 11 mM.

One strength of the current study is that all patients with invasive pneumococcal pneumonia who fulfilled the inclusion criteria at the study site during a 2-yr period were included, thus removing any sampling errors. There are also limitations

to the current study. First, the number of patients treated in OD was small and the patients were all identified retrospectively, while all but two of those treated in DID were identified prospectively. However, exactly the same procedure in handling the data was used, with an identical standardised case-report form, and no difference in the number of missing variables between the two groups was seen. For all patients, both prospectively and retrospectively included, the data used for severity-score calculations were mostly obtained from medical records and laboratory databases compiled by the medical staff in charge of the patient during the first 24 h from admission. It is therefore highly unlikely that the retrospective analysis of patients' data would produce a less reliable result than the prospectively assembled data set. It is also unlikely that the retrospective analysis of medical records would misclassify severe underlying conditions, such as cancer or immunosuppressive treatment, or outcome parameters, such as intensive care treatment and death. Secondly, the time from admission until antibiotic treatment is initiated has been shown to have a certain impact on mortality [36], but such data were not available for the patients in the current study. Thirdly, it could be argued that the current authors have strayed from the original publications when using creatinine instead of urea in calculations for PSI and CURB-65. However, the results for APACHE-II and mATS scores, where urea is not included, were quite consistent with those for PSI and CURB-65.

Different case-fatality rate in a subgroup of patients despite stratification for severity of illness

Patients admitted to OD had a higher proportion of severe underlying diseases than those treated in DID, were more frequently severely ill on admission according to severity scores and, accordingly, had a higher case-fatality rate. However, the difference in mortality remained even when patients belonging to identical severity score strata were compared. One probable reason for this difference is that the presence of a severe underlying disease, such as cancer, is not included in the CURB-65 or mATS score calculations, and may have an unwarrantedly low impact on the PSI and APACHE-II scores. Further, it is also possible that the pneumococcal disease in itself may differ between patients who are previously healthy and those who have an underlying severe illness. The dominating pneumococcal serotypes were 1, 14 and 4 in DID (where there were a low percentage of patients with severe underlying diseases) and 9V, 6A and 19F in OD (where severe underlying disease was very frequent). This is in accordance with the findings of a study where the current authors and others demonstrated that some serotypes, *e.g.* 1 and 7F, have a high invasive potential and behave like primary pathogens, mostly infecting previously healthy people [37]. In contrast, other sereotypes, *e.g.* 3, 4, 6A, 6B, 8, 9V, 14, 18C, 19F and 23F, seemed to be less invasive and behave like opportunistic pathogens infecting mostly people with chronic underlying disease.

The difference in case-fatality rates between the two groups indicates that neither APACHE-II nor the specific pneumonia severity scores are able to fully adjust for important differences between study populations, *e.g.* concerning severe underlying conditions. This, in turn, can create a risk of significant biases in noncontrolled multicentre studies of the prognosis of IPD, if sites with different population mixes are compared with each other. From a clinical viewpoint, this difference in mortality also enhances the importance of a thorough clinical assessment on admission, in addition to calculating severity scores, for the adequate management of and prognostic estimation in CAP patients.

In conclusion, the present study demonstrated that score systems developed for the assessment of community-acquired pneumonia could be used in defining severity of disease in pneumococcal pneumonia. CURB-65 is the most versatile score for use in a routine clinical setting and should be applied to all patients with community-acquired pneumonia in the emergency room. However, the current authors have also demonstrated that mortality within a certain score stratum may differ 3–4-fold depending on the patient group studied.

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