ORIGINAL ARTICLE

Community-acquired pneumonia as medical emergency: predictors of early deterioration

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ABSTRACT

Background Early organ dysfunction determines the prognosis of community-acquired pneumonia (CAP), and recognition of CAP as a medical emergency has been advocated.

Objective To characterise patients with 'emergency CAP' and evaluate predictors for very early organ failure or death.

Methods 3427 prospectively enrolled patients of the CAPNETZ cohort were included. Emergency CAP was defined as requirement for mechanical ventilation or vasopressor support (MV/VS) or death within 72 h and 7 days after hospital admission, respectively. To determine independent predictors, multivariate Cox regression was employed. The ATS/IDSA 2007 minor criteria were evaluated for prediction of emergency CAP in patients without immediate need of MV/VS.

Results 140 (4%) and 173 (5%) patients presented with emergency CAP within 3 and 7 days, respectively. Hospital mortality of patients presenting without immediate need of MV/VS was highest. Independent predictors of emergency CAP were the presence of focal chest signs, home oxygen therapy, multilobar infiltrates, altered mental status and altered vital signs (hypotension, raised respiratory or heart rate, hypothermia). The ATS/IDSA 2007 minor criteria showed a high sensitivity and negative predictive value, whereas the positive predictive value was low. Reduction to 6 minor criteria did not alter accuracy.

Conclusions Emergency CAP is a rare but prognostic relevant condition, mortality is highest in patients presenting without immediate need of MV/VS. Vital sign abnormalities and parameters indicating acute organ dysfunction are independent predictors, and the ATS/IDSA 2007 minor criteria show a high negative predictive value.

Key messages

What is the key question?

- Which parameters and scores predict mechanical ventilation, vasopressor support or death within 3 and 7 days in patients with community-acquired pneumonia (CAP) (emergency CAP)?

What is the bottom line?

- For the rare but prognostic event of emergency CAP, abnormalities of vital signs and parameters indicating acute organ dysfunction are independent predictors, and the ATS/IDSA 2007 minor criteria show a high negative predictive value.

Why read on?

- This large study characterises those patients with CAP who have the worst short-term prognosis in order to facilitate early identification and better management for this important CAP subgroup.

INTRODUCTION

In obvious contrast to medical and public perception and despite much progress in medicine and in critical care particularly, short-term mortality associated with community-acquired pneumonia (CAP) remains high. CAP mortality of hospitalised patients in Germany continues to be about 13%, rising to >35% in patients needing mechanical ventilation.[1] Even after exclusion of patients in nursing homes or those who are bedridden, mortality reaches about 7%, which matches mortality rates of other recognised medical emergency conditions such as ST-elevation myocardial infarction.[2 3]

Major causes of mortality include respiratory failure, severe sepsis/septic shock and underlying decompensated comorbidity.[4–7] Acute organ failure due to CAP occurs early in the disease, with 70% developing organ failure within the first 72 h after hospital admission.[4] Accordingly, the risk of death is highest within the first 3 days.[1] Recent studies have shown that timely management including a number of interventions significantly improves outcomes of patients with severe CAP.[8–15] Therefore, recognition of CAP as a medical emergency has been advocated to improve patient prognosis.[16]

The aim of this study was to characterise 'CAP as a medical emergency', defined as a need for mechanical ventilation, vasopressor use or death occurring within the first 72 h or 7 days after hospital admission, respectively, within a large prospective multicentre cohort of hospitalised patients with CAP (CAPNETZ). Additionally, we evaluated the American Thoracic Society/Infectious Diseases Society of America (ATS/IDSA) 2007 minor criteria for severe pneumonia[17] for predicting emergency CAP.

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PATIENTS AND METHODS

Patient population

Patients were recruited from the multicentre German Competence network for the study of CAP (CAPNETZ, http://www.capnetz.de). A detailed description of the CAPNETZ methodology is given elsewhere.[18] Criteria for inclusion in the study were age ≥18 years, a pulmonary infiltrate diagnosed by chest radiography, and at least one of the following criteria: history of fever (temperature ≥38.3°C), cough, production of purulent sputum or focal chest signs on auscultation. Exclusion criteria were acquired or therapeutically induced immune deficiency, active TB or possible nosocomial acquisition of infection. All clinical and vital signs and score parameters were evaluated at first contact after hospital admission. All patients were followed up according to a standardised protocol for 180 days and all clinical parameters were stored in an electronic database. To evaluate outcome parameters, all patients or their relatives were contacted either personally or by phone for structured interviews. Written informed consent was obtained from every patient before inclusion in the study, and the study was approved by the local ethical committees of each participating centre.

For this study, all patients admitted to hospital between 2007 and 2013 with available data on mechanical ventilation (MV), vasopressor support (VS) and death within the first 7 days after hospital admission as well as available 30-day mortality data were included.

Predefined endpoints and subgroup analyses

'Emergency CAP' was defined as requirement for MV (invasive or non-invasive, but excluding home ventilation), VS or death within 72 h or within 7 days after hospital admission, respectively.

Furthermore, a preplanned subgroup analysis compared patients meeting the emergency CAP criteria within 72 h after admission with all patients meeting the emergency CAP criteria within days 4–30 after admission.

Score definitions

The CRB-65 (C, mental confusion; R, respiratory rate ≥30/min; B, systolic blood pressure <90 mm Hg or diastolic blood pressure ≤60 mm Hg; 65, age ≥65 years), CURB (C, confusion, U, blood urea nitrogen ≥20 mg/dL, R, respiratory rate ≥30/min, B, systolic blood pressure <90 mm Hg or diastolic blood pressure ≤60 mm Hg) and PSI (Pneumonia Severity Index) scores were determined as described previously.[19 20]

The ATS/IDSA 2007 minor criteria for severe pneumonia[17] were evaluated for predicting emergency CAP; prediction was performed for all patients presenting without immediate need of MV/VS. The minor criterion 'hypotension requiring aggressive fluid resuscitation' was considered positive in patients presenting with systolic blood pressure <90 mm Hg and/or diastolic blood pressure ≤60 mm Hg. The minor criterion 'PaO_2/FiO_2 ratio ≤250' was met if one of the following was present: (1) PaO_2 <52 mm Hg while breathing room air or the pre-existing oxygen flow if receiving home oxygen therapy; (2) if no room air data were available, FiO_2 was calculated as supplemental oxygen in L/min ×0.03+0.21; (3) if no blood gas analysis was available the criterion was met if SaO_2 <86% while breathing room air or the pre-existing oxygen flow if receiving home oxygen therapy; (4) SaO_2/FiO_2 was <274 with supplemental oxygen.[21] The other minor criteria were calculated as described previously.[18]

In a predefined subgroup analysis the predictive value of adding one of the following supplemental minor criteria[22] was evaluated: pH <7.35, sodium <130 mmol/L, serum glucose <4.4 mmol/L, serum glucose >14 mmol/L.

Statistical analysis

Continuous variables are expressed as mean (±SD) or median (IQR), as appropriate, unless otherwise stated. Medians between groups were compared using the non-parametric Mann–Whitney test and qualitative variables were compared using the χ^2 test or Fisher's exact test in cases of small expected frequencies. Receiver operating characteristic curve analysis was used to determine the diagnostic properties of predictive parameters, and optimal cut-off values were calculated by the Youden Index. To evaluate the independent predictive value of parameters associated with emergency CAP, a multivariate Cox regression model with stepwise forward selection (inclusion level 0.05, exclusion level 0.1) was performed. Start and end dates for the time variable in the Cox regression model were day 1 and day 3 (for emergency CAP within 72 h) or day 1 and day 7 (for emergency CAP within 7 days) after hospital admission, respectively. To evaluate independent predictors for emergency CAP, all measured variables significantly associated with the endpoint in univariate analyses and present in >5% of patients were included in the model. For multivariate evaluation of the ATS/IDSA minor criteria, all nine criteria alone, and in a second analysis together with the four additional severity criteria, were included. Results are presented as HR and 95% CI. A p value of ≤0.05 (two-sided) was considered statistically significant. Statistical analyses were performed with SPSS V.22.0 and MedCalc V.13.2.2 software.

RESULTS

Overall, 140/3427 (4%) patients met the criteria for emergency CAP within 72 h after hospital admission, and 173 (5%) within 7 days (figure 1). Thirty-day mortality rates of these emergency patients with CAP were 17% and 27%, respectively. In contrast, mortality of non-emergency patients with CAP was significantly lower at 2% (p<0.001). Most patients (130/140 and 151/173, respectively) received MV/VS as the criterion for emergency CAP, but 10 patients in the former and 12 patients in the latter group died without having received MV/VS. Thirty-five of 130 (27%) and 56 of 151 (37%) patients receiving MV/VS within 72 h and 7 days, respectively, presented without immediate need of MV/VS on admission. Thirty-day mortality of patients receiving MV/VS within 7 days after admission but presenting without immediate need of MV/VS was 16/56 (29%), which was significantly higher than that of patients presenting with immediate need of MV/VS (8/95 (8%), p=0.002). The 30-day mortality rate of all patients fulfilling the emergency CAP definition within 7 days but presenting without immediate need of MV/VS was 49% (38/78). Of the 95 patients receiving immediate MV/VS, 29 (31%) immediately needed invasive ventilation or vasopressor treatment with a 30-day mortality of 24% (7/29), and 66 (69%) immediately received non-invasive ventilation (19/66 had chronic respiratory comorbidities, 8/66 needed invasive ventilation or vasopressor treatment in the course) with a 30-day mortality of 2% (1/66, p<0.001 vs invasive MV/VS).

Characteristics and predictors of emergency CAP within 72 h

The characteristics of these patients compared with all other patients with CAP are shown in table 1. In multivariate Cox regression analysis, home oxygen therapy, abnormal auscultation, multilobar infiltrates and abnormal vital signs were

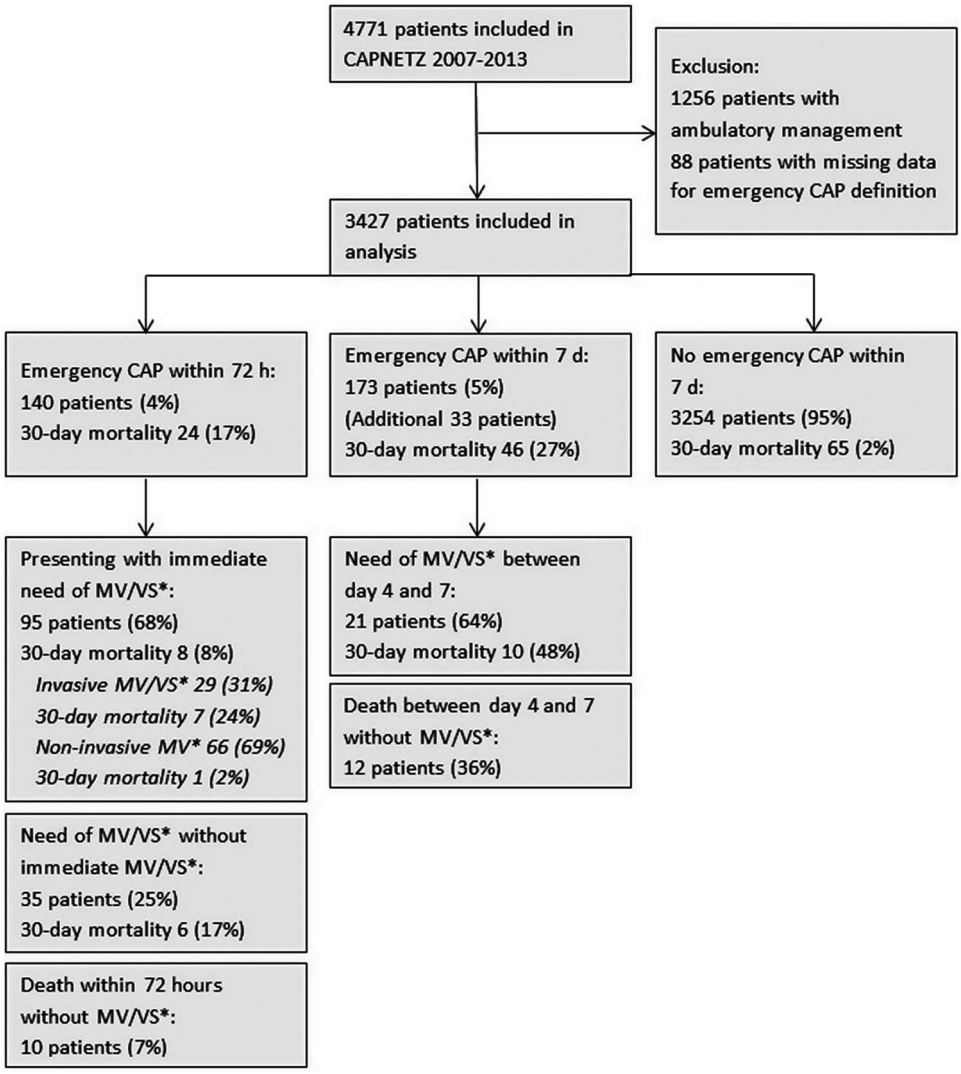

Figure 1 Flow chart showing features of community-acquired pneumonia (CAP) as an emergency (*MV/VS, mechanical ventilation and/or vasopressor support).

independent predictors of emergency CAP (table 2). In patients with emergency CAP a pathogen was more often detected as well as significantly more *H. influenzae* and less *M. pneumoniae* (online supplementary table S1); however, the possibility that more frequent microbiological testing was carried out in these patients cannot be excluded.

When the 140 patients presenting as emergency CAP within 72 h were compared with all patients meeting the same criteria within days 4–30, the latter were older, more obese and more often had chronic heart disease other than heart failure or malignancy (online supplementary table S2). On the other hand, early adverse outcome was associated with fewer prehospital antibiotics, tachycardia, smoking and pneumococcal CAP (online supplementary table S2). By multivariate Cox regression analysis, only higher heart rate and lower age were independent predictors for the emergency group (online supplementary table S3).

Characteristics and predictors of emergency CAP within 7 days

Thirty-three additional patients died or needed MV/VS between days 4 and 7 after hospital admission (figure 1). If these 33 patients were included in the emergency group, no major changes of univariate and multivariate comparisons or microbiological findings resulted apart from a history of chronic renal disease, which was another independent predictor in the multivariate Cox regression (table 3, online supplementary table S4).

Evaluation of ATS/IDSA 2007 minor criteria for predicting emergency CAP

If patients presenting with immediate need of MV/VS were excluded from the analysis, 45 patients developing emergency CAP within 72 h remained. Of these, all except four presented with at least one positive minor criterion (median 2).

Complete information on all nine minor criteria was available for 3049 patients. Significant differences between emergency and non-emergency patients with CAP were detected for oxygenation index, multilobar infiltrates, confusion, hypotension, urea and hypothermia (table 4). However, only confusion, hypotension and urea were identified as independent predictors by multivariate Cox regression analysis (table 4). The three criteria—white cell count <4000 cells/mm^3, platelets <100 000 cells/mm^3 and hypothermia <36°C—were detected only rarely among study patients. After inclusion of four additional criteria suggested in the literature[22] (pH <7.35, sodium <130 mmol/L, glucose <4.4 mmol/L, glucose >14 mmol/L), only pH was an independent predictor for emergency presentation (table 4). Predictive properties of the minor criteria are shown in table 5;

Table 1 Characteristics of patients according to emergency status within 72 h

Characteristics	Emergency 72 h (N=140)	Non-emergency (N=3287)	p Value
Demographics			
Age, median (range)	69 (19–90)	67 (18–102)	**0.047**
Male sex, N (%)	92 (66)	2002 (61)	0.25
Height (cm), median (range)	170 (147–198)	172 (133–202)	0.4
Weight (kg), median (range)	75 (37–180)	76 (30–217)	0.94
Body mass index, median (range)	25 (12–61)	26 (12–85)	0.75
Smoker, N (%)	41 (29)	905 (28)	0.48
Antibiotics within 4 weeks, N (%)	21 (15)	766 (23)	**0.02**
Influenza vaccination, N (%)	47 (34)	1191 (36)	0.84
Pneumococcal vaccination, N (%)	14 (10)	438 (13)	0.34
Clinical findings at presentation			
Focal chest signs, N (%)	127 (91)	2655 (81)	**0.003**
Cough, N (%)	123 (88)	2951 (90)	0.46
Purulent sputum, N (%)	76 (54)	1743 (53)	0.77
Fever, N (%)	82 (59)	2145 (65)	0.1
Comorbidities			
Chronic respiratory disease, N (%)	46 (33)	941 (29)	0.28
Home oxygen therapy, N (%)	32 (23)	214 (7)	**<0.001**
Extrapulmonary comorbidity, N (%)	98 (70)	1974 (60)	**0.02**
Congestive heart failure, N (%)	41 (29)	619 (19)	**0.002**
Other chronic heart disease, N (%)	54 (39)	1296 (39)	0.84
Chronic renal disease, N (%)	24 (17)	321 (10)	**0.004**
Chronic liver disease, N (%)	5 (4)	90 (3)	0.56
Malignant disease, N (%)	13 (9)	331 (10)	0.76
Cerebrovascular disease, N (%)	11 (8)	208 (6)	0.47
Other chronic neurological disease, N (%)	11 (8)	145 (4)	0.06
Diabetes mellitus, N (%)	34 (24)	601 (18)	0.07
Gastric tube feeding, N (%)	5 (4)	6 (0)	**<0.001**
Nursing home residency, N (%)	11 (8)	100 (3)	**0.002**
Vital signs			
Systolic blood pressure (mm Hg), median (IQR)	123 (35)	130 (29)	**0.028**
Diastolic blood pressure (mm Hg), median (IQR)	70 (22)	73 (15)	**<0.001**
Respiratory rate, median (IQR)	24 (8)	20 (6)	**<0.001**
Heart rate, median (IQR)	98 (28)	90 (21)	**<0.001**
Temperature (°C), median (IQR)	37.5 (1.6)	37.8 (1.7)	**0.009**
Multilobar infiltrate, N (%)	61 (44)	809 (25)	**<0.001**
Pleural effusion, N (%)	31 (22)	558 (17)	0.1
Altered mental status, N (%)	25 (18)	179 (5)	**<0.001**
CRB-65 score, mean	1.5	0.9	**<0.001**
CURB-65 score, mean	2.1	1.2	**<0.001**
PSI score risk class, mean	3.3	2.5	**<0.001**
30-Day mortality, N (%)	24 (17)	87 (3)	**<0.001**
180-Day mortality, N (%)	34 (24)	196 (6)	**<0.001**

Significant p values are shown in bold.
CRB-65, C, mental confusion; R, respiratory rate ≥30/min; B, systolic blood pressure <90 mm Hg or diastolic blood pressure ≤60 mm Hg; 65, age ≥65 years); CURB, C, confusion, U, blood urea nitrogen ≥20 mg/dL, R, respiratory rate ≥30/min, B, systolic blood pressure <90 mm Hg or diastolic blood pressure ≤60 mm Hg; PSI, Pneumonia Severity Index.

the optimal cut-off point was two minor criteria. If the minor criteria were reduced to the first six criteria (without white cell count <4000 cells/mm^3, platelets <100 000 cells/mm^3 and hypothermia <36°C), no difference resulted. For the 2268 patients with initial pH values available, the inclusion of pH <7.35 instead of the last three minor criteria did not change the predictions.

If emergency patients with CAP within 7 days after admission (without immediate need of MV/VS) were evaluated, the minor criteria 1–6 and hypothermia all were significantly associated with emergency presentation, and after multivariate analysis, oxygenation index, confusion, hypotension and urea persisted as predictive factors (online supplementary table S5). For predictive accuracy, no major changes resulted (online supplementary table S6).

DISCUSSION

The main findings of our study are (1) emergency CAP is rare but of major prognostic impact, occurring in 4% of patients within 72 h and 5% within 7 days after admission; (2) 37% of patients receiving MV/VS within 7 days presented without immediate need of MV/VS on admission but had a significantly higher 30-day mortality rate, which was highest in emergency CAP developing between days 4 and 7; (3) independent

Table 2 Multivariate Cox regression analysis of risk factors (significant in univariate analysis and present in >5% of patients) for CAP as an emergency within 72 h

Characteristics	HR (95% CI)	p Value
Demographics		
Age		0.94
Antibiotics within 4 weeks		0.19
Clinical findings at presentation		
Focal chest signs	**2.12 (1.14 to 3.94)**	**0.017**
Comorbidities		
Home oxygen therapy	**2.86 (1.89 to 4.32)**	**<0.001**
Extrapulmonary comorbidity		0.77
Congestive heart failure		0.54
Chronic renal disease		0.12
Vital signs		
Systolic blood pressure		0.38
Diastolic blood pressure	**0.97 (0.96 to 0.98)**	**<0.001**
Respiratory rate	**1.05 (1.03 to 1.08)**	**<0.001**
Heart rate	**1.02 (1.01 to 1.03)**	**<0.001**
Temperature	**0.71 (0.60 to 0.83)**	**<0.001**
Multilobar infiltrate	**1.91 (1.35 to 2.70)**	**<0.001**
Altered mental status	**2.54 (1.61 to 4.02)**	**<0.001**

Significant results are shown in bold.
CAP, community-acquired pneumonia.

predictors of emergency CAP within 72 h were the presence of focal chest signs, home oxygen therapy, multilobar infiltrates, altered mental status and altered vital signs (hypotension, raised respiratory or heart rate, hypothermia); (4) the ATS/IDSA 2007 minor criteria showed a high sensitivity and negative predictive value for prediction of emergency CAP without immediate need of MV/VS, whereas the positive predictive value was low.

Our data confirm the dramatic prognosis of patients with emergency CAP. Therefore, the need to identify those patients is reinforced. Patients needing immediate mechanical ventilation and/or presenting with septic shock, albeit obvious, do not have the highest risk of death. In particular, patients receiving immediate non-invasive ventilation had a remarkably low mortality rate of 2%, indicating that timely management of organ failure if detected immediately might improve diagnosis. Instead, the highest 30-day mortality rate was seen in patients presenting without immediate need of MV/VS both in the emergency group within 72 h after admission and in the group deteriorating within the first 7 days. This is consistent with reported findings suggesting that deterioration in the disease course and late intensive care unit (ICU) management are associated with the worst prognosis.[9 23 24] Thus, efforts to identify and define patients at highest risk of early deterioration are warranted in order to provide intensive management of those patients with the highest potential for an improved outcome.

Table 3 Multivariate Cox regression analysis of risk factors (significant in univariate analysis and present in >5% of patients) for emergency CAP within 7 days

Characteristics	HR (95% CI)	p Value
Demographics		
Age		0.37
Male sex		0.24
Antibiotics within 4 weeks		0.23
Clinical findings at presentation		
Focal chest signs	**2.10 (1.21 to 3.64)**	**0.008**
Comorbidities		
Home oxygen therapy	**2.59 (1.77 to 3.79)**	**<0.001**
Extrapulmonary comorbidity		0.70
Congestive heart failure		0.38
Chronic renal disease	**1.57 (1.04 to 2.37)**	**0.032**
Vital signs		
Diastolic blood pressure	**0.97 (0.96 to 0.99)**	**<0.001**
Respiratory rate	**1.05 (1.03 to 1.08)**	**<0.001**
Heart rate	**1.01 (1.01 to 1.02)**	**0.002**
Temperature	**0.73 (0.63 to 0.84)**	**<0.001**
Multilobar infiltrate	**2.06 (1.51 to 2.81)**	**<0.001**
Altered mental status	**2.74 (1.82 to 4.13)**	**<0.001**

Significant results are shown in bold.
CAP, community-acquired pneumonia.

Our approach of defining a subgroup of patients with CAP as emergency helps to target such interventions and presents a clinically more relevant approach than predicting 30-day mortality or ICU admission. Simple prediction of mortality does not automatically lead to accurate identification of patients needing intensive management strategies and is influenced by age, comorbidities and treatment restrictions. ICU admission is biased by admission policy and is highly dependent on individual physician decisions. Therefore, a management-based risk stratification approach has been advocated[7] and successfully implemented.[10]

Our data show that patients at highest risk were those presenting with altered vital signs and parameters of organ dysfunction on admission, whereas (except for renal comorbidity in the 7-day emergency group) comorbidities were not significant after multivariate analysis. This strengthens the concept of focusing on identification and management of acute organ failure in CAP[5 7] and emphasises the need for careful clinical evaluation and interpretation of vital sign abnormalities. The results of our study need validation in independent cohorts.

Of comorbidities, chronic renal and heart failure and current smoking were associated with emergency CAP in univariate analysis, whereas other cardiac disease, malignant disease and age were associated with poor outcome between days 4 and 30. This might indicate risk of early organ failure in patients with the former diseases and confirms a mortality risk with age and the latter diseases.[4 5 20 25]

Patients with antibiotic pretreatment before hospital admission seemed to have a lower rate of early deterioration, although this parameter was not an independent predictor after multivariate analysis. This parameter might have shown greater importance if antibiotic pretreatment for the current CAP (and not any pretreatment within 4 weeks) only had been considered, but these data were not available from our database. This would be in line with prior observations suggesting a possible role of prehospital antibiotic treatment for CAP in high-risk patients[26–28] and indicates the need for further study of such an approach. There are several additional variables which might be found to be protective against emergency CAP, such as time to first dose of antibiotics, administration of immunomodulatory therapies and combination antibiotic empirical treatment. Such variables should be included in future studies.

International guidelines recommend clinical scores to predict severe CAP. The 2007 ATS/IDSA rule is most widely recommended.[17 22 29 30] However, its predictive value is artificially inflated by the two major criteria mechanical ventilation and/or septic shock, which define critical disease rather than being risk factors for it. Accordingly, the application of the minor criteria

Table 4 Presence of ATS/IDSA 2007 minor criteria and additional suggested predictive parameters according to emergency status within 72 h (after exclusion of all patients presenting with major criteria)

Criteria	Emergency 72 h without immediate MV/VS (N=45)	Non-emergency (N=3287)	Univariate p value	Multivariate HR (Cox) (95% CI)	Multivariate p value (Cox)
ATS/IDSA minor criteria, N/N with data (%)					
PaO2/FiO2 ratio ≤250	17/45 (38)	660/3287 (20)	**0.003**		0.12
Respiratory rate ≥30	7/45 (16)	305/3287 (9)	0.15		0.11
Multilobar shadowing	17/44 (39)	809/3174 (25)	**0.047**		0.06
Confusion	9/45 (20)	179/3285 (5)	**<0.001**	2.92 (1.28 to 6.67)	**0.01**
Hypotension	17/45 (38)	704/3277 (21)	**0.008**	1.97 (1.04 to 3.74)	**0.036**
Urea ≥20 mg/dL	26/42 (62)	1005/3060 (33)	**<0.001**	2.62 (1.38 to 5.00)	**0.003**
White cell count <4000 cells/mm^3	0/45 (0)	42/3281 (1)	0.45		0.42
Platelets <100 000 cells/mm^3	2/44 (5)	59/3258 (2)	0.18		0.42
Hypothermia <36°C	2/45 (4)	39/3273 (1)	**0.05**		0.11
Additional criteria, N/N with data (%)					
pH <7.35	5/36 (14)	76/2386 (3)	**<0.001**	3.26 (1.12 to 9.48)	**0.03**
Sodium <130 mmol/L	4/43 (9)	225/3259 (7)	0.54		0.78
Glucose <4.4 mmol/L	3/43 (7)	75/3116 (2)	0.06		0.26
Glucose >14 mmol/L	2/43 (5)	113/3116 (4)	0.72		0.57

Significant p values are shown in bold.
ATS, American Thoracic Society; IDSA, Infectious Disease Society of America; MV/VS, mechanical ventilation and/or vasopressor support.

alone to predict the two major criteria has been used successfully[30] and complies with the concept of early management-based risk assessment. Recently, the prognostic performance of the minor criteria for prediction of MV/VS has been confirmed in a meta-analysis,[22] and their ability to improve outcome in severe CAP after implementation in the emergency room has been demonstrated.[10] Our data largely confirm these findings. After exclusion of patients presenting with immediate need of MV/VS, the first six minor criteria and hypothermia predicted the 7-day endpoint, but leucopenia, thrombopenia and hypothermia were only rarely present. If these three criteria were removed, the resulting six instead of nine criteria were equally accurate, in line with a recent meta-analysis.[22] Several additional parameters have been suggested for prediction of high risk (acidosis, hypoglycaemia, hyperglycaemia, hyponatraemia).[22 31] In our study, only acidosis independently predicted emergency CAP; however, its addition to the minor criteria did not significantly improve the overall prediction, which is in accordance with the recent meta-analysis.[22] The minor criteria showed excellent negative predictive values for emergency CAP, but positive predictive values remained very low.

A few other studies have evaluated prediction of early deterioration within 72 h. One study assessed risk factors for ICU admission within 72 h and also found vital parameter abnormalities associated with early deterioration.[31] However, unlike in our cohort, the additional risk factors hyponatraemia, hyperglycaemia, leucopenia and pleural effusion were predictors of early ICU admission. These authors proposed a new score for early ICU prediction (the Risk of Early Admission to the ICU index (REA-ICU)), which in a recent validation study showed no advantage over the ATS/IDSA 2007 minor criteria and other proposed scores for prediction of 72 h ICU or MV/VS prediction.[32] In that study including 850 patients with CAP, the minor criteria had the same area under the curve of 0.72 as seen in our cohort. Another study focused on patients with CAP dying within 48 h after hospital admission (without examining MV/VS), and found similar risk factors, such as altered mental status, multilobar pneumonia and systemic hypotension, but also additional factors, such as age, pneumococcal bacteraemia and discordant empirical antibiotic therapy, independently associated with early mortality.[33]

Recently, the addition of new biomarkers mirroring the status of the cardiopulmonary and stress regulation system, such as mid-regional-proadrenomedullin (MR-proADM), copeptin or cortisol, has been suggested to improve high-risk prediction.[7] One recent study demonstrated promising results in identifying high-risk patients by using MR-proADM with a prognostic area

Table 5 ROC characteristics and prognostic properties of minor criteria for emergency CAP within 72 h *presenting without immediate need of MV/VS*

Criteria	AUC (95% CI)	Cut-off point	Sensitivity (95% CI)	Specificity (95% CI)	PPV (95% CI)	NPV (95% CI)	+LR (95% CI)	−LR (95% CI)
ATS/IDSA minor criteria 1–9	0.72 (0.71 to 0.74)	1	93 (80 to 98)	31 (29 to 33)	1.8 (1.3 to 2.5)	99.7 (99 to 100)	1.34 (1.2 to 1.5)	0.24 (0.08 to 0.27)
		2	**68 (51 to 81)**	**66 (65 to 68)**	**2.7 (1.8 to 3.9)**	**99.3 (98 to 100)**	**2.01 (1.6 to 2.5)**	**0.49 (0.3 to 0.8)**
ATS/IDSA minor criteria 1–6	0.73 (0.71 to 0.74)	1	93 (80 to 99)	32 (30 to 33)	1.8 (1.3 to 2.5)	99.7 (99 to 100)	1.35 (1.2 to 1.5)	0.23 (0.08 to 0.7)
		2	**66 (49 to 80)**	**68 (66 to 69)**	**2.8 (1.8 to 4)**	**99.3 (99 to 100)**	**2.04 (1.6 to 2.6)**	**0.5 (0.3 to 0.8)**
ATS/IDSA minor criteria 1–6 and pH	0.73 (0.71 to 0.74)	1	94 (79 to 99)	28 (26 to 30)	1.9 (1.3 to 2.7)	99.7 (99 to 100)	1.3 (1.2 to 1.4)	0.22 (0.06 to 0.9)
		2	**69 (50 to 84)**	**63 (61 to 65)**	**2.7 (1.7 to 4)**	**99.3 (99 to 100)**	**1.86 (1.5 to 2.4)**	**0.5 (0.3 to 0.8)**

Bold values show the optimal cut-off point according to the Youden Index.
N Minor criteria 1–9: 3049; N minor criteria 1–6: 3084; N minor criteria 1–6+ pH: 2268.
ATS, American Thoracic Society; AUC, area under the curve; CAP, community-acquired pneumonia; IDSA, Infectious Disease Society of America; LR, likelihood ratio; MV/VS, mechanical ventilation and/or vasopressor support; NPV, negative predictive ratio; PPV, positive predictive ratio; ROC, receiver operating characteristic.

under the curve of 0.73.[34] However, further data on these markers are necessary and ideally, interventional trials should be performed to assess their additional value for management-based risk stratification.

Nevertheless, the risk prediction of scores, including the ATS/IDSA score, remains limited. Inflating scores with new variables has not led to substantial improvements of such predictions. In addition, complex scores might not be an ideal way of improving every day management of emergency CAP in busy emergency departments. Therefore, it appears that in addition to objective scoring, preferably with the ATS/IDSA 2007 minor criteria, initial and repeated clinical assessment of the criteria characteristic for emergency CAP, as identified in this study, might be the best way to meet the challenge of managing patients with emergency CAP. As septic organ dysfunction is a dynamic process,[6] clinical parameters of acute organ dysfunction, including the minor criteria of oxygenation, respiratory rate, confusion, hypotension and urea, should be re-evaluated regularly, at least daily, until clinical stability is reached.[23] Future studies evaluating genomic, transcriptomic and proteomic markers of pneumonia progression, enabling a better understanding of the pathophysiology of CAP progression, may lead to better and even individualised stratification and management of severe CAP to improve the prognosis of this disease.

This study has some limitations. As this was a retrospective evaluation of prospectively enrolled patients, data were not complete for all criteria. We were unable to provide serial measurements of clinical parameters and minor criteria for continuous risk assessment, and data on new cardiovascular or stress biomarkers. Comorbidity assessment was based on history only and was not verified by clinical investigations. Finally, this analysis did not take into account potential treatment restrictions. Treatment restrictions are not exclusion criteria in the CAPNETZ protocol, but only 3% of included patients were in nursing homes before CAP hospitalisation and the median age was 9 years lower than in the German nationwide CAP performance measurement cohort.[1] Therefore, most patients with treatment restrictions probably have not been included in the study.

In conclusion, patients meeting the criteria for emergency CAP are a small but important group with a considerable risk of death but with a high potential for prognostic improvement if early organ failure is treated. Patients deteriorating within the first 3–7 days without presenting an immediate need for MV/VS on admission have the worst prognosis. Vital sign abnormalities and parameters indicating acute organ dysfunction are the most important factors to consider, and careful clinical evaluation of patients initially and at follow-up should be supplemented by established scores like the ATS/IDSA 2007 minor criteria.

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