

Original Article

Validation of IDSA/ATS Guidelines for ICU Admission in Adults Over 80 Years Old With Community-Acquired Pneumonia



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ABSTRACT

Introduction: The 2007 IDSA/ATS guidelines for community-acquired pneumonia (CAP) recommended intensive care unit (ICU) admission for adults meeting severe CAP criteria. We aimed to validate the accuracy of IDSA/ATS criteria in patients ≥ 80 years old (very elderly patients, VEP) with CAP.

Methods: Prospective cohort study of VEP with CAP admitted to three Spanish hospitals between 1996 and 2019. We compared patients who did and did not require ICU admission. We also assessed factors independently associated with ICU admission, as well as the accuracy of severe CAP criteria for ICU admission and mortality. Major criteria include septic shock and invasive mechanical ventilation while minor criteria encompass other variables related to hemodynamics and respiratory insufficiency as well as level of consciousness, renal function, blood parameters indicative of sepsis and body temperature.

Results: Of the 2006 VEP with CAP, 519 (26%) met severe CAP criteria, while 204 (10%) required ICU admission. Concordance between severe CAP criteria and the decision to admit the patient to the ICU occurred in 1591 (79%) cases (k coefficient, 0.33), with a sensitivity of 75% and specificity of 80% in predicting ICU admission. All patients with invasive mechanical ventilation received care in ICUs, while 45 (44%) patients with septic shock—previously stabilized in the emergency room—did not. Thirty-day mortality of ICU-admitted patients with septic shock was lower than that of patients in wards (30% vs. 60%, $p = 0.013$). In contrast, patients with severe CAP and only minor criteria had similar mortality.

Conclusions: IDSA/ATS criteria for severe CAP predict ICU admission in VEP moderately well. While patients with septic shock and invasive mechanical ventilation warrant ICU admission, severe CAP without major severity criteria in VEP may be acceptably manageable in wards.

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Introduction

Over the last two decades, due to an increased life expectancy in many countries worldwide, the proportion of critically ill and

patients ≥ 80 years old (very elderly patients: VEP) has grown significantly.^{1,2} A higher proportion of VEP admitted to the ICU largely impacts healthcare resources and costs.

Community-acquired pneumonia (CAP) is the main cause of sepsis and presents in up to 71% of all critically ill VEP, with an ICU mortality rate of 17%.^{3,4} However, there are no specific recommendations for managing critically ill VEP with CAP. Moreover, diagnosing CAP in VEP is often difficult and results in frequent delays in antibiotic therapy initiation.⁵

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The most recent CAP guidelines⁶ issued by the Infectious Diseases Society of America/American Thoracic Society (IDSA/ATS) still recommend the use of the diagnostic criteria proposed in 2007⁸ in defining patients with severe CAP requiring ICU admission. This recommendation followed the validation of the criteria by several studies.^{7–10} However, these severity criteria have not been validated yet in VEP. We hypothesized that IDSA/ATS severity criteria are not appropriate to guide decisions regarding ICU admission in VEP with CAP. The aim of the study was therefore to validate the predictive ability of the 2007 IDSA/ATS criteria for severe CAP in identifying individuals in the VEP population admitted to the ICU.

Methods

Study design and patients

This is a multicenter observational study based on the analysis of data obtained from a prospective registry of hospitalized patients with CAP. Three teaching hospitals from Spain participated in the study: Hospital Clinic of Barcelona (1996–2019) [$n=1635$]; Hospital Universitario Cruces (2005–2019) [$n=627$] and Hospital La Fe of Valencia (2012–2019) [$n=309$]. We prospectively included all hospitalized patients aged ≥ 80 years with CAP and compared those admitted to the ward and ICU within 24 h of hospitalization. Exclusion criteria were: (1) age < 80 years; (2) severe immunosuppression (neutropenia after chemotherapy or hematopoietic transplant; drug-induced immune suppression in solid organ transplant or cytotoxic therapy; oral corticosteroid treatment with at least 20 mg prednisone or equivalent per day for at least two weeks; HIV infection); (3) active tuberculosis; and (4) patients with do-not-resuscitate (DNR) orders at the time of ICU admission. Pneumonia was defined as a new pulmonary infiltrate on a chest X-ray at hospital admission, with symptoms and signs of lower respiratory tract infection.¹¹ More details about data collection and microbiological diagnosis are described in the [Supplementary Material](#).

For publication purposes, the study was approved by the IRB of our institutions (Register: HCP2009/5451). Written informed consent was waived due to the non-interventional design of the study.

Definitions

A prior episode of pneumonia was defined as that occurring within the prior 12 months. Severe CAP was defined when at least one major (septic shock or a need for invasive mechanical ventilation) or 3 minor criteria of the 2007 IDSA/ATS guidelines were present ([Supplementary Table S1](#)). IDSA/ATS criteria for severe CAP requiring ICU admission¹¹ used the working definition of “direct ICU admission”, i.e., admission directly from the emergence room in the first 24 h after consultation to the hospital. Prior antibiotic treatment was considered when patients had taken antibiotics in the previous month. Polymicrobial pneumonia was defined as more than one pathogen being identified as the causative agent. Septic shock was defined as a systolic blood pressure of < 90 mmHg and peripheral hypoperfusion with the need for vasopressors for > 4 h after fluid resuscitation. Appropriateness of empirical antibiotic treatment was defined in all patients based on multidisciplinary guidelines for CAP management.^{11,12}

Outcomes and study groups

The primary outcome was ICU admission. We divided the study population into two groups: patients hospitalized in the ward and patients admitted to the ICU, including intermediate care units. The secondary outcome was 30-day mortality.

Statistical analysis

We reported the number and percentage of patients as categorical variables, the median (Q1; Q3) as continuous variables with non-normal distributions, and the mean (standard deviation [SD]) as continuous variables with normal distributions. Categorical variables were compared using the chi-squared test or Fisher’s exact test, whereas continuous variables were compared using the t -test or non-parametric Mann–Whitney U test.

We also performed univariable and multivariable logistic regression analyses¹³ to identify variables predictive of ICU admission. Factors showing an association in the univariable analyses ($p < 0.10$) were incorporated into the multivariable regression model. Final variable selection was performed using the backward stepwise selection method (likelihood ratio) ($p_{in} < 0.05$, $p_{out} > 0.10$). Odds ratios (ORs) and their 95% confidence intervals (CIs) were calculated. Single collinearity was evaluated using the Pearson correlation (r) and multicollinearity was examined by means of the variance inflation factor (VIF). Discrimination and calibration were assessed by area under the receiver operating characteristic curve (AUC) and the Hosmer–Lemeshow test, respectively. For the assessment of internal validity, we used ordinary nonparametric bootstrapping with 1000 bootstrap samples and bias-corrected, accelerated 95% CIs.¹⁴ We used the multiple imputation method¹⁵ for missing data in the analyses to identify variables predictive of ICU admission ([Supplementary Table S2](#)). To determine the ability of IDSA/ATS severe CAP criteria to predict ICU admission, we determined sensitivity, specificity and positive and negative likelihood ratio,¹⁶ along with 95% CIs. The coincidence between the predictive rule and the clinical decision for ICU admission was assessed with the $kappa$ coefficient of agreement.¹⁷ The univariate association of the predictive rule and the severity criteria with ICU admission is also expressed as the relative risk and the 95% CI. The level of significance was set at 0.05 (two-tailed), and all analyses were performed using IBM SPSS Version 26.0 (IBM Corp., Armonk, NY, USA).

Results

Study population

During the study period, 10,742 patients with CAP visited the emergency room and 2571 (24%) were hospitalized VEP without a DNR order, of whom 2006 (78%) patients, with a median (Q1; Q3) age of 85 (82; 88) were included in the analysis. 1802 (90%) were admitted to the general ward while 204 (10%) to the ICU ([Fig. 1](#)).

The IDSA/ATS criteria identified 519 (26%) of this series of patients as having severe CAP: 58 (11%) had major severity criteria only; 84 (16%) had major and at least one minor severity criteria; and, in the absence of major criteria, 377 (73%) had three or more minor severity criteria. Of those 519 patients with severe CAP, 154 (30%) were admitted to the ICU. Only 50 (3%) of the 1487 patients who were defined as not having severe CAP received ICU admission.

Patient characteristics

The main clinical characteristics of the study population are shown in [Table 1](#). Patients admitted to the ICU were younger, more often males, and more frequently smoked and abused alcohol. Conversely, when compared to those patients who were not admitted to ICU, those admitted to the ICU had received the influenza vaccine less frequently; were less likely to have chronic neurological diseases; and presented higher rates of diabetes mellitus, altered mental status, higher levels of creatinine, C-reactive protein and serum glucose, and a lower platelet count and PaO_2/FiO_2 . Additionally, when compared to non-ICU-admitted patients, patients

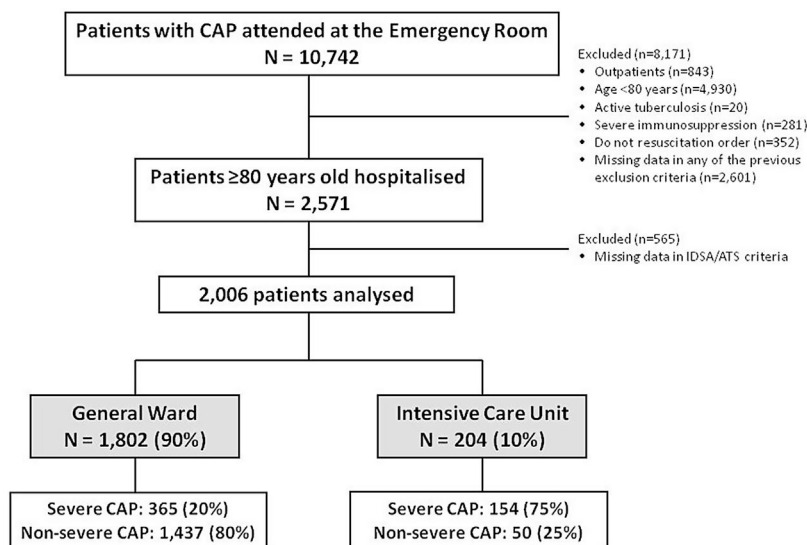


Fig. 1. Flow chart of the study population.

admitted to the ICU had higher PSI score; presented severe CAP criteria more frequently; and experienced more pulmonary and extra-pulmonary complications, longer hospital stay and higher 30-day mortality.

Microbial etiology

ICU-admitted patients had a higher rate of etiological diagnosis than non-ICU patients (Supplementary Table S3). However, we did not find any significant differences regarding the relative proportion of causative pathogens between ICU and non-ICU patients.

Predictors of ICU admission

Logistic regression analysis indicated that male sex, absence of chronic neurological disease, respiratory rate ≥ 30 breath/min, systolic blood pressure < 90 mmHg, serum creatinine ≥ 1.5 mg/dL, serum glucose ≥ 200 mg/dL, $\text{PaO}_2/\text{FiO}_2 < 250$, pleural effusion, multilobar infiltration and septic shock were independently associated with ICU admission (Table 2). The AUC for the ICU admission prediction model was 0.86 (95% CI 0.84–0.89). Internal validation of the final model demonstrated robust results (Supplementary Table S4).

Severe CAP and prediction of ICU admission (Table 3)

Concordance between IDSA/ATS criteria for severe CAP and ICU admission occurred in 1591 (79%) cases; the kappa coefficient was 0.33 ($p < 0.001$). The predictive rule overestimated the number of patients who would be admitted to the ICU, i.e., 365 (20%) patients who were not admitted to the ICU had severe CAP criteria, whereas only 50 (25%) ICU-admitted patients had non-severe CAP.

Sensitivity and specificity of IDSA/ATS criteria for severe CAP in identifying patients admitted to ICUs were 75% and 80%, respectively. Severe CAP was 3.73 times more frequent among ICU-admitted patients compared to those not admitted to the ICU. Likewise, the probability that ICU-admitted patients had non-severe CAP was only 0.31, when compared to non-ICU patients. Compared with patients with non-severe CAP, patients with severe CAP had an 8.82-fold higher relative risk of ICU admission.

Severe CAP and prediction of mortality

Thirty-day mortality was higher among ICU-admitted patients than in those not admitted to the ICU ($p < 0.001$; Table 1). Differences in mortality between groups remained unchanged when analyzing patients with severe and non-severe CAP separately (Table 3). Table 5 shows the association between the predictive rule and mortality. Severe CAP and the presence of either of the two major severity criteria had the strongest association with mortality. All minor severity criteria were also significantly associated with 30-day mortality. Sensitivity, specificity, positive and negative likelihood ratios, and the risk ratio of severe CAP criteria in predicting 30-day mortality were similar to those of patients admitted to the ICU.

Severity criteria and outcome variables for patients requiring ICU admission or not

Major severity criteria had the highest association with ICU admission, particularly invasive mechanical ventilation. However, 45 (44%) patients with septic shock who were initially managed and stabilized in the emergency department did not require subsequent ICU admission. In patients with septic shock, 72 (71%) did not receive invasive mechanical ventilation, and these had similar median PSI scores irrespective of their likelihood of ICU admission. However, 30-day mortality was lower in patients with septic shock admitted to the ICU (8 [30%] vs. 27 [60%], $p = 0.013$).

In contrast, the 377 patients with severe CAP defined by the presence of ≥ 3 minor criteria in the absence of major criteria, less often were admitted to the ICU (Table 4). In this subset of patients, while the PSI score was lower in ICU-admitted patients (138 [123; 154] vs. 145 [130; 160], $p = 0.045$), 30-day mortality was similar (12 [21%] vs. 53 [17%], $p = 0.37$).

Discussion

The definition of severe CAP in the 2007 IDSA/ATS guidelines is moderately accurate for predicting both ICU admission and mortality in patients aged 80 years and older, with 25% of the patients with severe CAP criteria (mainly based on the presence ≥ 3 minor criteria) being admitted to the ICU.

Integrating certain key characteristics of VEP patients (e.g., frailty, malnutrition, multiple comorbidities, polypharmacy, etc.)

Table 1
Characteristics of the study population by site of care.

Variable	Patients not in the ICU (N= 1802)	Patients in the ICU (N= 204)	p-Value
Age, years, median (Q1; Q3)	84 (82; 88)	83 (81; 85)	<0.001
Male sex, n (%)	1048 (58)	139 (68)	0.006
Current smoker, n (%)	100 (6)	21 (11)	0.006
Current alcohol consumer, n (%)	99 (6)	21 (11)	0.005
Previous antibiotic, n (%)	382 (22)	36 (19)	0.408
Influenza vaccine, n (%)	999 (67)	89 (57)	0.009
Pneumococcal vaccine, n (%)	348 (24)	37 (23)	0.984
Previous inhaled corticosteroids, n (%)	267 (20)	41 (23)	0.305
Previous systemic corticosteroids, n (%)	47 (4)	11 (7)	0.104
Previous episode of pneumonia (last year), n (%)	253 (19)	25 (14)	0.116
Comorbidities, n (%) ^a	1412 (78)	152 (75)	0.311
Chronic respiratory disease	744 (42)	80 (41)	0.720
Chronic cardiovascular disease	511 (28)	45 (23)	0.073
Diabetes mellitus	439 (25)	63 (31)	0.038
Neurological disease	370 (21)	28 (14)	0.033
Chronic renal disease	238 (13)	29 (14)	0.664
Chronic liver disease	39 (2)	3 (1)	0.794
Nursing-home, n (%)	141 (8)	13 (7)	0.498
Confusion, n (%)	357 (20)	72 (36)	<0.001
Respiratory rate, breaths/min, median (Q1; Q3)	24 (18; 28)	30 (24; 36)	<0.001
Heart rate, beats/min, median (Q1; Q3)	92 (80; 105)	100 (84; 115)	<0.001
Systolic blood pressure, mmHg, median (Q1; Q3)	135 (119; 154)	127 (100; 150)	<0.001
Diastolic blood pressure, mmHg, median (Q1; Q3)	70 (61; 80)	65 (57; 79)	<0.001
Temperature, °C, median (Q1; Q3)	37.3 (36.6; 38.0)	37.0 (36.3; 38.0)	0.157
Serum creatinine, mg/dL, median (Q1; Q3)	1.2 (0.9; 1.5)	1.5 (1.1; 2.2)	<0.001
C-reactive protein, mg/dL, median (Q1; Q3)	15.7 (7.6; 25.7)	21.1 (9.1; 28.5)	0.008
White blood cell count, cells/mm ³ , median (Q1; Q3)	12,810 (9300; 17,390)	13,350 (9000; 19,100)	0.436
Lymphocytes, cells/mm ³ , median (Q1; Q3)	924 (560; 1350)	828 (417; 1440)	0.294
Glucose level, mg/dL, median (Q1; Q3)	132 (111; 170)	159.5 (115; 232)	<0.001
Platelet count, platelets/mm ³ , median (Q1; Q3)	256 (189; 530)	241 (165; 314)	<0.001
PaO ₂ /FiO ₂ , median (Q1; Q3)	276 (239; 314)	233 (189; 275)	<0.001
PSI score, median (Q1; Q3)	111 (93; 132)	135 (120; 159)	<0.001
Severe CAP, n (%)	365 (20)	154 (75)	<0.001
Only ≥1 major criteria	18 (1)	40 (20)	<0.001
Only ≥3 minor criteria	320 (18)	57 (28)	<0.001
≥1 major criteria and ≥3 minor criteria	27 (1)	57 (28)	<0.001
Bacteremia, n (%) ^b	124 (9)	27 (17)	0.003
Pleural effusion, n (%)	193 (11)	36 (18)	0.002
Multilobar, n (%)	372 (21)	90 (44)	<0.001
ARDS, n (%)	44 (3)	35 (18)	<0.001
Acute renal failure, n (%)	557 (33)	116 (58)	<0.001
Septic shock, n (%)	45 (2)	57 (28)	<0.001
Appropriate empiric treatment, n (%)	1494 (93)	150 (82)	<0.001
Length of hospital stay, days, median (Q1; Q3)	6 (5; 9)	12 (8; 18)	<0.001
Invasive mechanical ventilation, n (%) ^c	0 (0)	70 (34)	<0.001
30-Day mortality, n (%) ^d	128 (7)	53 (26)	<0.001

Abbreviations: ARDS indicates acute respiratory distress syndrome; CAP, community-acquired pneumonia; FiO₂, fraction of inspired oxygen; ICU, intensive care unit; PaO₂, partial pressure of arterial oxygen; PSI, pneumonia severity index; Q1, first quartile; Q3, third quartile. Percentages calculated on non-missing data. p-Values marked in bold indicate numbers that they are statistically significant within the 95% confidence limit.

^a Possibly >1 comorbidity.

^b Calculated only for patients with blood samples (1323 in the ward group and 159 in the ICU group).

^c Patients who initially received non-invasive ventilation but needed subsequently intubation were included in the invasive mechanical ventilation group.

^d Calculated only for patients with 30-day follow-up (1776 in the ward group and 202 in the ICU group).

in their enhance the clinical decision-making process, in particular regarding certain life-support treatments such as the use of IMV.¹⁸ In addition, ICU admission in VEP with CAP might largely vary due to local hospital practices. In our study, 10% of VEP with CAP required ICU admission, which is in line with prior studies.^{19,20} Developing tools that support decision-making processes beyond the “crude age” is necessary.

Some of the variables independently associated to a higher likelihood of ICU admission in our cohort largely overlap with IDSA/ATS criteria for severe CAP. Others, such as male sex and hyperglycemia are frequently associated with ICU admission both in the general population and VEP, while pleural effusion makes part of the “Risk of Early Admission to ICU” (REA-ICU) score.^{21,22} Patients with a chronic neurological disease, which is a frequent cause of disability in VEP, often face exclusion from ICU admission.

In our cohort, the IDSA/ATS criteria for severe CAP moderately predicted ICU admission (75% sensitivity, 80% specificity). In a meta-analysis, the same criteria had a pooled sensitivity of 84% and a specificity of 78% for predicting ICU admission in the general adult population.²³ The presence of major criteria, particularly receiving invasive mechanical ventilation, was a main determinant in deciding whether ICU admission. It is worth mentioning that in spite that our study is not the first at attempting to assess the prediction ability of IDSA/ATS criteria with regards to the likelihood of ICU admission, there is an inherent flaw in this approach, namely that receiving invasive mechanical ventilation as one of the major criteria is per se associated with ICU admission. Hence the potential usefulness of minor criteria over major criteria in certain populations. In the case of VEP, patients are less likely to receive endotracheal intubation and mechanical ventilation than younger patients. Moreover, not all patients that receive invasive

Table 2

Significant univariable logistic regression analyses for variables associated with ICU admission and independent predictors of ICU admission determined by multivariable logistic regression analysis (N = 2006).

Variable	Univariable ^a			Multivariable ^{a,b,c}		
	OR	95% CI	p-Value	OR	95% CI	p-Value
Male sex	1.54	1.13–2.10	0.006	1.59	1.11–2.30	0.012
Chronic cardiovascular disease	0.71	0.50–1.01	0.056	–	–	–
Diabetes mellitus ^d	1.44	1.05–1.97	0.022	–	–	–
Neurological disease	0.63	0.42–0.95	0.026	0.38	0.23–0.61	<0.001
Confusion	2.30	1.69–3.12	<0.001	–	–	–
Respiratory rate ≥ 30 breaths/min	3.39	2.53–4.56	<0.001	2.78	1.93–4.01	<0.001
Heart rate ^e			<0.001			–
<60 beats/min	1.00	0.23–4.29	0.996	–	–	–
60–100 beats/min	1.00	–	–	–	–	–
≥ 100 beats/min	1.79	1.34–2.40	<0.001	–	–	–
Systolic blood pressure < 90 mmHg	5.55	3.59–8.57	<0.001	2.14	1.21–3.78	0.009
Diastolic blood pressure ≥ 140 mmHg ^d	4.05	1.74–9.42	0.001	–	–	–
Temperature ^f			0.008			–
<36 °C	2.22	1.34–3.66	0.002	–	–	–
36–38 °C	1.00	–	–	–	–	–
≥ 38 °C	1.15	0.84–1.58	0.374	–	–	–
Serum creatinine ≥ 1.5 mg/dL	2.59	1.93–3.47	<0.001	1.51	1.06–2.14	0.022
C-reactive protein ≥ 15 mg/dL	1.40	1.04–1.88	0.027	–	–	–
White blood cell count ^g			0.030			–
<4000 cells/mm ³	2.06	1.17–3.64	0.013	–	–	–
4000–10,000 cells/mm ³	1.00	–	–	–	–	–
$\geq 10,000$ cells/mm ³	1.06	0.75–1.50	0.749	–	–	–
Lymphocytes < 724 cells/mm ³	1.21	0.90–1.63	0.198	–	–	–
Glucose level ≥ 200 mg/dL	2.67	1.94–3.67	<0.001	2.18	1.49–3.18	<0.001
Platelet count, <100,000 platelets/mm ³	2.46	1.20–5.02	0.014	–	–	–
PaO ₂ /FiO ₂ < 250	3.63	2.69–4.90	<0.001	2.31	1.62–3.29	<0.001
Pleural effusion	1.85	1.26–2.72	0.002	1.79	1.11–2.89	0.018
Multilobar	3.03	2.25–4.09	<0.001	2.60	1.81–3.73	<0.001
Septic shock	15.14	9.89–23.17	<0.001	9.26	5.40–15.87	<0.001

Abbreviations: CI indicates confidence interval; FiO₂, fraction of inspired oxygen; ICU, intensive care unit; OR, odds ratio; PaO₂, partial pressure of arterial oxygen. Data are shown as estimated ORs (95% CIs) of the explanatory variables in the ICU admission group. The OR represents the odds that the presence of ICU admission will occur given exposure of the explanatory variable, compared to the odds of the outcome occurring in the absence of that exposure. The p-value is based on the null hypothesis that all ORs relating to an explanatory variable equal unity (no effect).

^a The variables analyzed in the univariable analyses were sex, antibiotic use in the last week, chronic pulmonary disease, chronic cardiovascular disease, chronic renal disease, chronic liver disease, diabetes mellitus, neurological disease, confusion, respiratory rate, heart rate, systolic blood pressure, diastolic blood pressure, temperature, creatinine, C-reactive protein, lymphocytes, white blood cell count, glucose level, platelet count, PaO₂/FiO₂, pleural effusion, multilobar infiltration, and septic shock.

^b Hosmer–Lemeshow goodness-of-fit test, $p = 0.800$. Area under the ROC curve, AUC = 0.86 (95% CI 0.84–0.89).

^c Adjusted for period of admission and center.

^d Diabetes mellitus was excluded from the multivariable analysis because of collinearity with glucose level, while diastolic blood pressure was omitted because systolic blood pressure collinearity.

^e The p-value corresponds to differences between the three groups (<60 beats/min, 60–100 beats/min, or ≥ 100 beats/min).

^f The p-value corresponds to differences between the three groups (<36 °C, 36–38 °C, or ≥ 38 °C).

^g The p-value corresponds to differences between the three groups (<4000 cells/mm³, 4000–10,000 cells/mm³, or $\geq 10,000$ cells/mm³).

mechanical ventilation are admitted to the ICU. Patients can be intubated by the emergence services outside the hospital or early after they arrive to the emergence room and only require invasive mechanical ventilation during a short period before they are either admitted to the ICU or even the ward. In any case, whereas in the first IDSA/ATS criteria validation study conducted by Liapikou et al.⁷ authors concluded that the need for ICU admission derived from minor severity criteria alone was uncertain, our study suggest that it might be the opposite in the case of VEP.

Most patients with severe CAP treated outside of the ICU had ≥ 3 minor severity criteria in the absence of major criteria, and they did not therefore, require active life support measures. Thus, using the IDSA/ATS minor criteria to identify severe CAP early for aggressive emergency department resuscitation resulted in lower hospital mortality and ICU admission rates, as well as less inappropriately delayed ICU admissions.²⁴ Once these VEP patients with minor severity criteria have been stabilized in the emergency room, our results do not support that further admission to the ICU would have resulted in reduced mortality.

Available evidence shows that well-selected VEP with CAP admitted to the ICU present better outcomes than those who are not.^{25,26} In our cohort, patients with severe CAP not admitted to an ICU were older than those admitted to an ICU, with a similar PSI score (which includes age, comorbidities and acute severity of pneumonia). In a multicenter study by Andersen et al., 29.6% of VEP were denied ICU admission.²⁵ Our findings suggest that chronological age, as patients with DNR were excluded, play a relevant in the decision to assign some of these patients with severe CAP to the ward rather than ICU. With available data, it seems advisable to use the IDSA/ATS criteria as an aid to clinical judgment that can be further complemented with other biomarkers and the patients baseline quality of life until more evidence is gathered in VEP.^{27,28}

The prediction of severe CAP criteria for 30-day mortality was similar to that for ICU admission in our VEP.

The strengths of this study include the prospective design, large sample size, participation of three hospitals, and comprehensive data collection over an extended time period, which also might pose a limitation due to potential historical bias. However, our work has

Table 3
Infectious Diseases Society of America/American Thoracic Society guidelines criteria for severe CAP and operative indices to predict ICU admission.

Variable	n/N (%)		p-Value	Sensitivity % (95% CI)	Specificity % (95% CI)	Likelihood ratio		Risk ratio (95% CI)
	Patients not in the ICU (N=1802)	Patients in the ICU (N=204)				Positive (95% CI)	Negative (95% CI)	
Severe CAP	365/1802 (20)	154/204 (75)	<0.001	75 (69–82)	80 (78–82)	3.73 (3.30–4.20)	0.31 (0.24–0.39)	8.82 (6.52–11.95)
Non-severe CAP	1437/1802 (80)	50/204 (25)						
Major criteria^a								
Received invasive mechanical ventilation	0/1802 (0)	70/204 (34)	<0.001	34 (28–41)	100 (100–100)	–	0.66 (0.59–0.73)	7.24 (5.74–9.13)
Septic shock	45/1802 (2)	57/204 (28)	<0.001	28 (22–34)	98 (97–98)	11.19 (7.78–16.09)	0.74 (0.68–0.81)	7.23 (5.74–9.13)
≥1 major criteria	45/1802 (2)	97/204 (48)	<0.001	48 (40–55)	98 (97–98)	19.04 (13.79–26.29)	0.54 (0.47–0.61)	11.90 (9.59–14.76)
Minor criteria^a								
Hypotension requiring aggressive fluid resuscitation	52/1776 (3)	25/189 (13)	<0.001	13 (8–18)	97 (96–98)	4.52 (2.87–7.11)	0.89 (0.85–0.95)	3.74 (2.62–5.32)
Respiratory rate ≥30 breaths/min	413/1718 (24)	96/181 (53)	<0.001	53 (45–61)	76 (74–78)	2.21 (1.88–2.59)	0.62 (0.53–0.72)	3.08 (2.35–4.06)
PaO ₂ /FiO ₂ ≤ 250	430/1410 (31)	117/189 (62)	<0.001	62 (55–69)	69 (67–72)	2.02 (1.76–2.31)	0.55 (0.46–0.66)	3.10 (2.35–4.08)
Temperature < 36 °C	93/1773 (5)	18/185 (10)	0.012	10 (5–14)	95 (94–96)	1.85 (1.15–3.00)	0.95 (0.91–1.00)	1.79 (1.15–2.80)
White blood cell count < 4000 cells/mm ³	93/1798 (5)	20/204 (10)	0.007	10 (5–14)	95 (94–96)	1.90 (1.20–3.01)	0.95 (0.91–1.00)	1.82 (1.19–2.77)
Platelet count < 100,000 platelets/mm ³	20/1166 (2)	7/147 (5)	0.025	5 (1–9)	98 (98–99)	2.78 (1.19–6.45)	0.97 (0.93–1.01)	2.38 (1.24–4.59)
Uremia (creatinine level > 1.5 mg/dL or BUN 20 mg/dl or greater)	500/1798 (28)	100/202 (50)	<0.001	50 (42–57)	72 (70–74)	1.78 (1.52–2.08)	0.70 (0.61–0.80)	2.29 (1.77–2.96)
Multilobar involvement	372/1798 (21)	90/204 (44)	<0.001	44 (37–51)	79 (77–81)	2.13 (1.78–2.55)	0.70 (0.62–0.80)	2.63 (2.04–3.40)
Mental confusion	357/1795 (20)	72/202 (36)	<0.001	36 (29–43)	80 (78–82)	1.79 (1.46–2.20)	0.80 (0.72–0.89)	2.02 (1.55–2.64)
≥3 minor criteria	347/1802 (19)	114/204 (56)	<0.001	56 (49–63)	81 (79–83)	2.90 (2.49–3.39)	0.55 (0.47–0.64)	4.25 (3.29–5.48)
Only ≥3 minor criteria	320/1802 (18)	57/204 (28)	<0.001	28 (22–34)	82 (80–84)	1.57 (1.24–2.00)	0.88 (0.80–0.96)	1.68 (1.26–2.23)

Abbreviations: BUN indicates blood urea nitrogen; CAP, community-acquired pneumonia; FiO₂, fraction of inspired oxygen; ICU, intensive care unit; PaO₂, partial pressure of arterial oxygen. p-Values marked in bold indicate numbers that are statistically significant within the 95% confidence limit.

^a Percentages calculated only for patients with or without severe CAP. For some patients the data (minor criteria) were not available.

Table 4
Characteristics of patients with severe and non-severe CAP in relation to hospital site of care.

Variable	Patients with severe CAP			Patients with non-severe CAP		
	Patients not in the ICU (N=365)	Patients in the ICU (N=154)	p-Value	Patients not in the ICU (N=1437)	Patients in the ICU (N=50)	p-Value
Age, years, median (Q1; Q3)	86 (83; 90)	83 (81; 85)	<0.001	84 (82; 87)	83 (81; 86)	0.087
PSI score, median (Q1; Q3)	146 (131; 161)	143 (128; 163.5)	0.713	103 (91; 120)	120 (101; 125)	0.011
Length of hospital stay, days, median (Q1; Q3)	8 (6; 12)	13 (9; 20)	<0.001	6 (4; 8)	10 (7; 15)	<0.001
30-Day mortality, n (%)	80 (22)	48 (32)	0.020	48 (3)	5 (10)	0.032
Major severity criteria for severe CAP, n (%)						
Septic shock	45 (12)	57 (37)	<0.001	–	–	–
Invasive mechanical ventilation	0 (0)	70 (45)	<0.001	–	–	–
≥1 major criteria	45 (12)	97 (63)	<0.001	–	–	–
Minor severity criteria for severe CAP, n (%)						
Hypotension requiring aggressive fluid resuscitation	43 (12)	25 (17)	0.109	9 (1)	0 (0)	>0.999
Respiratory rate ≥ 30 breaths/min	206 (61)	81 (59)	0.740	207 (15)	15 (34)	0.001
PaO ₂ /FiO ₂ ≤ 250	209 (68)	100 (71)	0.486	221 (20)	17 (35)	0.011
Temperature < 36 °C	51 (14)	16 (11)	0.396	42 (3)	2 (4)	0.396
White blood cell count < 4000 cells/mm ³	46 (13)	20 (13)	0.913	47 (3)	0 (0)	0.403
Platelet count < 100,000 platelets/mm ³	12 (5)	6 (6)	0.734	8 (1)	1 (2)	0.344
Uremia (creatinine level > 1.5 mg/dL or BUN 20 mg/dl or greater)	226 (62)	91 (60)	0.663	274 (19)	9 (18)	>0.999
Multilobar involvement	187 (51)	76 (49)	0.695	185 (13)	14 (28)	0.002
Mental confusion	197 (54)	67 (44)	0.038	160 (11)	5 (10)	0.794
≥3 minor criteria	347 (95)	114 (74)	<0.001	–	–	–
Only ≥3 minor criteria	320 (88)	57 (37)	<0.001	–	–	–

Abbreviations: BUN indicates blood urea nitrogen; CAP, community-acquired pneumonia; FiO₂, fraction of inspired oxygen; ICU, intensive care unit; PaO₂, partial pressure of arterial oxygen; PSI, pneumonia severity index; Q1, first quartile; Q3, third quartile. Percentages calculated on non-missing data. p-Values marked in bold indicate numbers that are statistically significant within the 95% confidence limit.

Table 5
Association of the predictive rule of severe CAP and other indices with 30-day mortality ^a

Variable	n/N (%)		p-Value	Sensitivity % (95% CI)	Specificity % (95% CI)	Likelihood ratio		Risk ratio (95% CI)
	Patients alive at 30 days (N = 1797)	Patients dead at 30 days (N = 181)				Positive (95% CI)	Negative (95% CI)	
Severe CAP	389/1797 (22)	128/181 (71)	<0.001	71 (64–78)	78 (76–80)	3.27 (2.87–3.72)	0.37 (0.30–0.47)	6.82 (5.04–9.25)
Non-severe CAP	1408/1797 (78)	53/181 (29)						
Major criteria^b								
Received invasive mechanical ventilation	41/1797 (2)	28/181 (15)	<0.001	15 (10–21)	98 (97–98)	6.78 (4.30–10.60)	0.87 (0.81–0.92)	5.06 (3.66–7.00)
Septic shock	52/1797 (3)	50/181 (28)	<0.001	28 (21–34)	97 (96–98)	9.55 (6.68–13.64)	0.75 (0.68–0.82)	7.02 (5.42–9.08)
≥1 major criteria	78/1797 (4)	63/181 (35)	<0.001	35 (28–42)	96 (95–97)	8.02 (5.97–10.77)	0.68 (0.61–0.76)	6.96 (5.40–8.96)
Minor criteria^b								
Hypotension requiring aggressive fluid resuscitation	59/1765 (3)	18/172 (10)	<0.001	10 (6–15)	97 (96–98)	3.13 (1.89–5.18)	0.93 (0.88–0.98)	2.82 (1.83–4.35)
Respiratory rate ≥ 30 breaths/min	420/1707 (25)	87/164 (53)	<0.001	53 (45–61)	75 (73–77)	2.16 (1.83–2.55)	0.62 (0.53–0.73)	3.04 (2.28–4.06)
PaO ₂ /FiO ₂ ≤ 250	461/1435 (32)	85/141 (60)	<0.001	60 (52–69)	68 (65–70)	1.88 (1.61–2.19)	0.59 (0.48–0.72)	2.86 (2.08–3.95)
Temperature < 36 °C	92/1760 (5)	19/170 (11)	0.001	11 (6–16)	95 (94–96)	2.14 (1.34–3.41)	0.94 (0.89–0.99)	2.06 (1.33–3.19)
White blood cell count < 4000 cells/mm ³	92/1793 (5)	20/181 (11)	0.001	11 (6–16)	95 (94–96)	2.15 (1.36–3.41)	0.94 (0.89–0.99)	2.07 (1.35–3.16)
Platelet count < 100,000 platelets/mm ³	21/1184 (2)	6/127 (5)	0.040	5 (1–9)	98 (97–99)	2.66 (1.10–6.48)	0.97 (0.93–1.01)	2.36 (1.14–4.87)
Uremia (creatinine level > 1.5 mg/dL or BUN 20 mg/dl or greater)	509/1792 (28)	87/180 (48)	<0.001	48 (41–56)	72 (69–74)	1.70 (1.44–2.01)	0.72 (0.62–0.83)	2.16 (1.64–2.85)
Multilobar involvement	383/1793 (21)	75/181 (41)	<0.001	41 (34–49)	79 (77–81)	1.94 (1.60–2.36)	0.74 (0.66–0.84)	2.34 (1.78–3.09)
Mental confusion	348/1790 (19)	79/180 (44)	<0.001	44 (36–51)	81 (79–82)	2.26 (1.87–2.73)	0.70 (0.61–0.79)	2.83 (2.15–3.72)
≥ 3 minor criteria	352/1797 (20)	107/181 (59)	<0.001	59 (52–67)	80 (79–82)	3.02 (2.59–3.52)	0.51 (0.43–0.61)	4.79 (3.63–6.31)
Only ≥ 3 minor criteria	311/1797 (17)	65/181 (36)	<0.001	36 (29–43)	83 (81–84)	2.08 (1.67–2.58)	0.78 (0.69–0.87)	2.39 (1.80–3.17)

Abbreviations: BUN indicates blood urea nitrogen; CAP, community-acquired pneumonia; FiO₂, fraction of inspired oxygen; ICU, intensive care unit; PaO₂, partial pressure of arterial oxygen. p-Values marked in bold indicate numbers that are statistically significant within the 95% confidence limit.

^a Calculated only for patients with 30-day follow-up (n = 1978).

^b Percentages calculated only for patients with or without severe CAP. For some patients the data (minor criteria) were not available.

several limitations. First, we did not record data on baseline quality of life, frailty, and/or functional status, which might have had an impact on clinical decisions regarding ICU admission. Second, relevant variables concerning the management of septic shock were not collected, e.g., dosage and duration of vasopressors. Third, it should be reminded that the IDSA/ATS criteria for indicating direct ICU admission in cases of severe CAP entailed admission to the ICU within 24 h from hospitalization, and therefore our study does not provide data on the ability of IDSA/ATS criteria to predict ICU admission at a later phase during hospital admission. Fourth, blood urea nitrogen (BUN) level was not systematically determined in our population; therefore, we used serum creatinine level as a surrogate, as we have done in previous studies.^{7,29} Fifth, we used the physicians' decision for ICU admission as the gold standard, as this reflected actual clinical practice. However, the variability of clinicians' judgment and the frequent constraints on the availability of ICU beds may have influenced site-of-care decisions. Finally, serum lactate, which is currently part of the definition of septic shock, was not systematically registered until recent years.

Conclusion

The IDSA/ATS criteria for severe CAP predict ICU admission in VEP moderately well. While our results indicate that patients with invasive mechanical ventilation and those with septic shock should be allocated to the ICU even when they have been stabilized previously, severe CAP not fulfilling either of those major severity criteria might be managed acceptably in wards.

Availability of data

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

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Conflict of interests

The authors declare that they have no competing interest.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at [doi:10.1016/j.arbres.2022.08.012](https://doi.org/10.1016/j.arbres.2022.08.012).

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