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Severity assessment in community-acquired pneumonia

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ABSTRACT: In current guidelines for the management of adults with community-acquired pneumonia (CAP), the triaging decision about hospitalization or intensive care unit (ICU) admission, and, as a consequence, selection of initial antimicrobial treatment is largely based on the assessment of pneumonia severity.

The proposed severity criteria are mainly derived from studies determining predictors of adverse outcome. These include age, male sex, comorbidity, acute respiratory failure, severe sepsis and septic shock, extension of radiographic infiltrates, bacteraemia and CAP through several different pathogens such as *Streptococcus pneumoniae*, *Staphylococcus aureus*, Gram-negative enteric bacilli (GNEB), and signs of disease progression within the first 48–72 h. In addition, prediction rules and need for a complicated course in ambulatory and hospitalized patients, for the individual risk of death have been developed which may be helpful in determining the patient who might require hospitalization or intensive care, respectively.

Risk classifications such as the scores developed by FINE *et al.* [40] are not only useful for identifying low risk patients who might safely be treated as outpatients, but apparently they will also play a major role in the evaluation of processes and outcomes of care for patients with CAP. Recent investigations have provided objective criteria for the definition of severe CAP requiring ICU admission. Whether the detection of infiltrates in the chest radiographs of patients with acute lower respiratory tract infection (LRTI) suggestive of mild pneumonia has an independent prognostic impact which fundamentally affects the concept of mild LRTI remains to be seen.

Based on objective criteria for severity assessment it will be possible to define interventions aimed at reducing hospital admission rates, define a risk-adapted antimicrobial treatment regimen, reduce costs for antimicrobial treatment and supportive measures, shorten hospital stay, and, thereby, improve the quality of care for patients with community-acquired pneumonia.

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Current guidelines for the treatment of patients with community-acquired pneumonia (CAP) are based on estimations of pneumonia severity which allow a risk-adapted approach to the decision about the treatment setting and the selection of initial empiric antimicrobial regimen [1–4]. The framework of severity assessment includes outpatient, hospitalized, and intensive care unit (ICU) pneumonia which corresponds to mild, moderate, and severe pneumonia. In particular, the guidelines of the American Thoracic Society (ATS) [1], the European Respiratory Society (ERS) [2, 3], and of the Infectious Disease Society of America (IDSA) [4] all agree in that severe CAP represents a pneumonia syndrome of its own which requires a distinct approach to diagnosis and treatment. This concept is also based on increasing evidence that severe CAP is more frequently associated with bacteraemia and distinct micro-organisms such as *Legionella* spp., Gram-negative enteric bacilli (GNEB), and *Pseudomonas aeruginosa* [5, 6].

Thus, the assessment of severity has become one of the most important issues in the management of patients presenting with CAP. In the following, the authors review the evidence from the recent literature with regards to prognostic factors, prognostic rules and severity criteria and their implications for clinical decision making. At the same time, emphasis will also be placed on explaining unresolved critical issues with respect to severity assessment.

Detecting mild pneumonia

Pneumonia is usually considered to represent a more serious illness than nonpneumonic acute lower respiratory tract illness such as acute bronchitis generally requiring antimicrobial treatment. If this holds true for mild pneumonia also, then the first step of severity assessment of a patient with symptoms of lower respiratory tract infection (LRTI) would be identical to the diagnostic

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evaluation for the presence of pneumonia. Otherwise, it would be more practical to restrict the diagnostic work-up of such patients to the assessment of severity of LRTI regardless of the potential presence of pneumonia in order to decide on which patient would require empiric antimicrobial treatment at all.

The ERS guidelines are based on the recognition that it may be very difficult in clinical practice to differentiate bronchitis and mild pneumonia. Therefore, an effort to differentiate acute bronchitis from pneumonia by a chest radiograph is only recommended in patients presenting with focal chest signs, the single clinical sign with the best predictive potential for the presence of pneumonia [7]. In fact, LRTI represents a spectrum ranging from mild bronchial to overwhelming parenchymal infection. Single clinical signs as well as diagnostic rules consisting of a set of criteria do not provide satisfactory performances in predicting the presence of pneumonia [8–11]. Chest radiographs are also only of limited value in the imaging of mild infiltrates [12, 13]. Moreover, since only every 10th or 20th patient with LRTI is expected to have true pneumonia [14], thus resulting in a low prevalence, the positive predictive value of any diagnostic rule will be low. Thus, a sharp distinction will not be possible in every case of mild LRTI. On the other hand, diagnostic rules have been shown to achieve acceptable negative predictive values [15]. Therefore, in the absence of clinical signs such as fever, tachypnoea, tachycardia, cough, expectoration and rales, pneumonia is improbable. Otherwise, the presence or absence of pneumonia can only be determined more reliably by a chest radiograph.

Up to the present day, however, no study has assessed whether the presence of infiltrates visible in the chest radiographs of patients with symptoms of mild LRTI has any implications in terms of outcome as compared to patients without infiltrates but similar clinical symptoms. This would be a pragmatic and clinically meaningful way to obviate the somewhat academic distinction between acute bronchitis and mild pneumonia. Moreover, no study has investigated whether a strategy which generally requires a chest radiograph to confirm pneumonia in patients with equivocal clinical features is superior to a strategy which is restricted to a clinical decision about the indication for empiric antimicrobial treatment. Evidently, both questions are of eminent importance in order to define an adequate strategy of diagnostic work-up and severity assessment in patients presenting with symptoms compatible with mild LRTI.

Risk factors for a complicated course of CAP

Around 80% of LRTI thought to represent true pneumonia are mild and can be treated on an outpatient basis [16]. However, in patients without obvious reasons for immediate hospitalization, the triaging of outpatients for hospital admission may be difficult. Therefore, a scoring system was derived from a retrospective chart review and validated prospectively [17]. In the derivation protocol, patients with a predefined disease complication present during the initial evaluation which required immediate hospitalization were excluded. The remaining patients were classified as hospitalization necessary or unnecessary. Independent predictors for the need for hospitalization and their relative weights were: 1) serious comorbid illness (3 points), 2) pre-existing lung disease (2), 3) multilobar infiltrates (2), 4) observed or likely aspiration (2), and 5) symptom duration <7 days or >28 days (1). Patients with low risk scores of 0–2 points rarely had complications (2% in both derivation and validation population) whereas patients with high scores ≥6 points had frequent complications (69% in derivation and 67% in validation population). Patients with intermediate scores 3–5 had complications in 19% and 25%, respectively. These data impressively show that simple clinical and radiological data can be helpful in the severity and risk assessment of ambulatory patients.

A limited but probably important proportion of patients initially judged to have mild pneumonia require hospitalization during the course of the disease because of the failure to respond to the initial empirical antimicrobial treatment or even due to clinical deterioration. In one study, five variables were found to predict treatment failure of patients initially assigned to ambulatory treatment [18].

Table 1. – Risk factors for a complicated course of community-acquired pneumonia (including death) according to the American Thoracic Society guidelines for the management of patients with community-acquired pneumonia

Premorbid epidemiological and historical factors
Age >65 yrs
Suspicion of aspiration (gastric or oropharyngeal secretions)
Congestive heart failure
COPD, bronchiectasis
Diabetes mellitus
Chronic alcohol abuse
Malnutrition
Chronic renal failure
Chronic liver disease of any aetiology
Hospitalization during the prior 12 months
Previous splenectomy
Altered mental status
Physical findings
Temperature >38.3°C
Respiratory rate ≥30·min^{-1}
Systolic blood pressure <90 mmHg, diastolic blood pressure <60 mmHg
Extrapulmonary involvement (septic arthritis, meningitis, *etc*.)
Mental confusion or decreased level of consciousness
Laboratory findings
Leukocytosis >30×10^9·L^{-1} or leukopenia <4×10^9·L^{-1}
Hematocrit <30% or haemoglobin <9 g·dL^{-1}
P_{a,O_2} <60 mmHg or P_{a,CO_2} >50 mmHg at F_{I,O_2} 0.21
Blood urea nitrogen ≥20 mg·dL^{-1} or creatinine ≥1.2 mg·dL^{-1}
Radiographic findings
>1 lobe involvement
Presence of cavity
Rapid radiographic spread
Presence of pleural effusion
Others
Requirement for mechanical ventilation
Evidence for sepsis or organ dysfunction (metabolic acidosis, increased prothrombin or partial thromboplastin time, decreased platelets, presence of fibrin split products)

COPD: chronic obstructive pulmonary disease; P_{a,O_2}: oxygen tension in arterial blood; P_{a,CO_2}: carbon dioxide tension in arterial blood; F_{I,O_2}: inspiratory oxygen fraction. Adapted from [1].

These included: 1) age >65 yrs; 2) the presence of comorbid illness; 3) fever (>38.3°C); 4) immunosuppression; and 5) the presence of high-risk aetiologies (including *S. aureus*, GNEB, aspiration, and postobstructive pneumonia). The risk of treatment failure increased linearly with the number of risk factors present. However, the results of this study are hampered by two important issues: 1) in view of different susceptibility to opportunistic pathogens, patients with severe immunosuppression should not be classified as having CAP; instead, these patients require a different approach to diagnosis and treatment [19]; 2) the aetiology is not known at the initial clinical evaluation of the patient and, therefore, can not form part of the initial risk assessment. Nevertheless, the crucial role of age and comorbidity remains evident.

The ATS guidelines have outlined a variety of factors that increase the risk for a complicated course for CAP (including death) and recommended that hospitalization should be strongly considered when multiple risk factors are present [1]. These factors are listed in table 1. The selection of risk factors was based on prognostic studies and clinical expertise. In fact, in a multicentre retrospective analysis of outcomes in patients with CAP, a linear correlation was observed between the number of risk factors according to these ATS guidelines and a variety of outcome measures, including mortality, admission at the ICU, mean hospitalization time, and mean cost [20].

Table 2. – Assessment of the need for hospitalization according to the German guidelines for the management of patients with community-acquired pneumonia

Premorbid epidemiological and historical factors
Age >65 yrs
Unstable home situation
Comorbidity
COPD or other structural lung disease
Cardiac disease
Renal disease
Hepatic disease
Diabetes mellitus
Alcohol abuse
Malnutrition
Immunosuppression (*e.g.* by corticosteroids)
Physical findings
Respiratory rate >30·min^{-1}
Systolic blood pressure <90 mmHg, diastolic blood pressure <60 mmHg
Mental confusion or decreased level of consciousness
Extrapulmonary involvement (septic arthritis, meningitis, *etc*.)
Radiographic findings
Multilobar and/or bilateral infiltrates
Lobar infiltrates or cavities
Pleural effusions
Laboratory findings
Leukocytosis >30×10^9·L^{-1} or leukopenia <4×10^9·L^{-1}
P_{a,O_2} <60 mmHg or S_{a,CO_2} <90% at F_{I,O_2} 0.21
Parameters indicating renal failure

COPD: chronic obstructive pulmonary disease; P_{a,O_2}: oxygen tension in arterial blood; S_{a,CO_2}: arterial oxygen saturation; F_{I,O_2}: inspiratory oxygen fraction. Adapted from [21]. According to these guidelines, hospitalization should be seriously considered in the presence of at least ≥2 adverse premorbid epidemiological and historical factors or one adverse physical finding (or, if available, one radiographic or laboratory finding).

In view of these findings, the German guidelines for the management of CAP have proposed an assessment of the need for hospitalization based on those factors in the list of ATS criteria available after the first clinical evaluation without any further laboratory or radiographic evaluation (table 2) [21]. On the other hand, the ERS guidelines have proposed to consider hospitalization in the presence of: 1) risk factors for severity, 2) risk factors for particular

Table 3. – Criteria for hospitalization according to the European Respiratory Society guidelines

Consideration of hospitalization	
Risk factors for severity	Risk factors for particular micro-organisms
Age >65 yrs	*Streptococcus pneumoniae*
Institutionalized patients	*Streptococcus pneumoniae*, GNEB, *Staphylococcus aureus*, anaerobes
Alcoholism	GNEB, *Legionella* spp.
Comorbidity	*Streptococcus pneumoniae*,
COPD	*Haemophilus influenzae*,
Cardiovascular disease	GNEB
Neurological diseases	
Diabetes mellitus	
Chronic liver or renal failure	
Recent viral infection	
Hospital admission within the previous year	*Streptococcus pneumoniae* (especially penicillin-resistant strains in some areas)
Hospital admission within the previous 2–4 weeks	GNEB
Recent treatment with penicillin or other antibiotics	*Streptococcus pneumoniae* (especially penicillin-resistant strains in some areas), other resistant micro-organisms
Aspiration	GNEB, *Staphylococcus aureus*, anaerobes
Recommendation of hospitalization	
Signs of immediate severity	
Home consultation	
Chest pain	
Confusion	
Drowsiness	
Tachycardia ≥125 bpm	
Temperature <35°C or ≥40°C	
Respiratory rate ≥30·min^{-1}	
Cyanosis	
Blood pressure <90/60 mmHg	
Complications	
Suspected pleural effusion or cavitation	
Metastatic infection	
Home management apparently impossible	
Vomiting	
Social exclusion	
Extreme poverty	
Dependency	
Poor likelihood of good compliance	
Altered mental status	

COPD: chronic obstructive pulmonary disease; GNEB: Gram-negative enteric bacilli.

micro-organisms typically associated with more severe pneumonia, (as defined in table 2, respectively), and 3) failure of first-line antimicrobial treatment [2]. Furthermore, hospitalization is clearly recommended in the presence of signs of immediate severity, complications, and other factors which render home management impossible. As is evident from table 3, most risk factors of severity refer to epidemiological characteristics and comorbid conditions. However, the link of these risk factors for severity and the presence of distinct micro-organisms seems debatable. For example whether CAP in nursing home residents is associated with a distinct microbial pattern is a subject of controversy [6], and whether ambulatory treatment failures are due to resistant micro-organisms in a significant proportion of the cases has not been determined.

Predicting death from pneumonia

Prognostic factors associated with death from pneumonia have been continuously studied in diverse patient populations, and, as outlined in detail in recent reviews covering this subject, more than 40 corresponding predictors in multivariate analyses could be identified [6, 19]. The adverse independent prognostic factors reported in the last decade are listed in table 4 [22–36]. A meta-analysis comprising of 122 studies dealing with the investigation of prognostic factors found ten independent predictors of death, including male gender, diabetes mellitus, neoplastic disease, neurologic disease, tachypnoea, hypotension, hypothermia, leucopenia, bacteraemia, and multilobar infiltrates, as well as pleuritic chest pain as a protective factor [37].

From a clinical point of view, the authors advocate that it seems useful to arrange these variables similar to the acute physiology and chronic health evaluation (APACHE) score into factors reflecting acute pneumonia related-illness and those reflecting the underlying health state [6, 19]. The former would be further divided into clinical signs and symptoms, laboratory, radiographic, microbiological and oxygenation parameters, whereas the later would include age, sex, referral (home or nursing-home), comorbidity and steroid pretreatment. A third group of parameters would represent evolutionary parameters reflecting disease progression. These factors differ in that they are not available at initial assessment but indicate prognosis during the course of disease. Again, these factors would be divided into clinical, radiographic, and treatment-associated parameters as well as other complications.

If the variety of factors found to be associated with death are examined, it appears that the main general denominators of prognosis include age, male sex, comorbidity, acute respiratory failure, severe sepsis and septic shock, extension of radiographic infiltrates, bacteraemia and CAP through several different pathogens such as *S. pneumoniae*, *S. aureus*, GNEB, and signs of disease progression within the first 48–72 h.

Risk score assessment

FINE *et al.* [38] have elaborated risk scores for patients with CAP. In a previous report, a pneumonia (disease-specific) prognostic index was derived from around 350 hospitalized patients and validated in more than 14,000 patients of the Medisgroups Comparative Hospital Database. This index included six predictors with an integer value directly proportional to the magnitude of its coefficient in a multivariate mortality model: 1) age >65 yrs +1 point, 2) pleuritic chest pain -2 points, 3) vital sign abnormality +2 points, 4) altered mental status +2 points, 5) high-risk aetiology +2 points, and 6) neoplastic disease +4 points. Patients were categorized into five risk classes. The index performed particularly well in classifying low-risk patients (classes I and II). The strength of this prognostic index is clearly its relative simplicity. It can successfully be applicated *e.g.* in studies comparing different treatment settings in nursing home residents with pneumonia [39]. Conversely, again the inclusion of aetiologic information precludes utilization of this score for clinical decision making within the initial evaluation of the patient.

Table 4. – Independent prognostic factors associated with death from community-acquired pneumonia in studies originating from the last decade including both the general and the intensive care unit treated populations

Population	Reference
General	
Respiratory rate $\geq 30 \cdot min^{-1}$	24–26
Systolic blood pressure $\leq$80 mmHg or <90 mmHg	24–26, 28
Diastolic blood pressure <60 mmHg	24–26
Blood urea nitrogen >7 $mmol \cdot L^{-1}$	24–26
Heart rate $\geq$90 bpm	28
Mental confusion	24–26
Low lymphocyte count	23
Low serum albumin	23
LDH $\geq 260\ U \cdot L^{-1}$	28
Bilateral pleural effusions	29
Elderly	
Temperature $\leq 37^{\circ}C$	30
Respiratory rate $\geq 30 \cdot min^{-1}$	30
Number of affected lobes $\geq$3	30
Bedridden state	30
ICU-treated general	
Age	33, 36
Anticipated death within 4–5 yrs	33, 36
SAPS >12 or >13	32, 33
Bilateral infiltrates	33
Requirement for mechanical ventilation	33, 36
Septic shock	31–34, 36
Involvement >1 lobe	36
Rapid radiographic spread	31
Inadequate or ineffective intial antimicrobial treatment	31, 34
Nonpneumonia related complications	34
Nonaspiration pneumonia	36
Bacteraemia	34
Streptococcus pneumoniae	32
Gram-negative enteric bacilli	32
Pseudomonas aeruginosa	33
ICU-treated elderly	
Septic shock	35
Acute renal failure	35
Rapid radiographic spread	35

LDH: lactate dehydrogenase; SAPS: Simplified Acute Physiology Score; ICU: intensive care unit.

In a subsequent study comprising a derivation and validation population of >50,000 patients together derived from the Medisgroups and Port cohorts, a two-step risk score was developed [40]. In a first step, the patient with a very low mortality risk (risk class 1) is identified by age <50 yrs, lack of comorbidity, and the absence of vital sign abnormalities. In a second step, risk classes II–V are calculated summing up points assigned to age, comorbid conditions, as well as vital sign abnormalities, and diverse epidemiological, laboratory, oxygenation and radiographic features recorded within the first 48 h after the primary clinical evaluation (table 5). It is noteworthy, that in this risk score age determines the risk class assignment to the largest extent. Additional factors with an exceptionally high impact on the risk score (30 points) include neoplastic disease and mild acidosis.

The first two risk classes were associated with a very low risk of mortality of <1%, whereas risk classes III–V were associated with a 2.8, 8.2, and 29.2 and 1.2, 9.0, and 27.1% mortality in the derivation and validation cohorts, respectively. The authors recently validated this rule in an elderly population with CAP. Mortality rates for risk classes II–V (risk class I was absent by definition) were 0, 2.7, 7.5, and 30.3%, respectively [41]. Thus, Fine′s classification proved to provide excellent predictions of risk also in this elderly European population.

Fine′s study was primarily interested in identifying the patient at low risk who might be safely treated on an outpatient basis. The most useful clue for the practitioner is the fact that a patient with risk class I has a risk of mortality of <1% and therefore, is the ideal candidate for ambulatory treatment. Although patients with risk classes II and III also have a very low risk of death from CAP, the assignment into these classes requires a tedious calculation and this might not be suitable in routine practice.

Table 5. – Criteria used in the severity assessment model for community-acquired pneumonia (risk classes II–V)

Criterion	Points
Age	Age (yrs)
Females	-10
Nursing home residency	10
Comorbidity	
Neoplastic	30
Liver	20
Congestive heart failure	10
Cerebrovascular disease	10
Renal disease	10
Vital sign abnormality	
Mental confusion	20
Respiratory rate ≥30·min^{-1}	20
Systolic blood pressure <90 mmHg	20
Temperature <35 or ≥40°C	15
Tachycardia ≥125 bpm	10
Laboratory abnormalities	
Blood urea nitrogen ≥11 mmol·L^{-1}	20
Sodium <130 mmol·L^{-1}	20
Glucose ≥250 mg·dL^{-1}	10
Haematocrit <30%	10
Radiographic abnormalities	
Pleural effusion	10
Oxygenation parameter	
Arterial pH <7.35	30
P_{a,O_2} <60 mmHg	10
S_{a,O_2} <90%	10

P_{a,O_2}: oxygen tension in arterial blood; S_{a,O_2}: arterial oxygen saturation. Point scoring system: risk class I: age <50, no comorbidity, no vital-sign abnormality; risk class II: ≤70 points; risk class III: 71–90 points; risk class IV: 91–130 points; risk class V: >130 points.

Conversely, this classification may prove very useful in further studies assessing processes of care and medical outcomes. Accordingly, the authors recently evaluated the management of patients with CAP admitted to a primary care hospital. It was found that principal conceptual weaknesses in this particular setting which might be subject to intervention were: 1) the hospitalization of patients with mild pneumonia at low risk of mortality; 2) a lack of association between microbial investigation and severity of CAP; 3) antimicrobial overtreatment of patients with nonsevere CAP; 4) inadequate antimicrobial treatment particularly in patients with severe CAP; and 5) an increased number of primary treatment failures and duration of hospitalization [42].

When using this risk score in routine practice, a note of caution should be made. Although mortality rates in risk classes I–III do not exceed 3%, they are not zero. Accordingly, single patients initially assigned to risk class I and II may even eventually require ICU admission [40, 41]. Thus, it is important to realize that patients with CAP and also at low risk of death should be re-examined clinically for possible unexpected deterioration. In this regard, a recent study provided very useful information about the time course of stability after the initiation of initial empiric antimicrobial treatment [43]. In hospitalized patients, the median time to overall clinical stability was 3 days for the most lenient definition of stability and 7 days for the most conservative definition. Time to stability was clearly correlated to initial severity. Once stability was achieved, clinical deterioration requiring ICU treatment occurred in <1% of cases. Similarly, in the recent series of severe CAP it was found that 80% of patients requiring ICU treatment were admitted within 24 h, and an additional 15% within 72 h [44]. Overall, these findings indicate that in patients with initially mild CAP treated on an outpatient basis, most deteriorating courses will occur within the first 24–72 h after the initiation of empiric antimicrobial treatment. Thus, any ambulatory treatment should prompt a reassessment of pneumonia severity and the clinical course within this time period.

Only recently, another interesting prediction rule for mortality from severe CAP treated in ICUs has been proposed [36]. In this study of 472 eligible patients with severe CAP, the following six variables available at initial evaluation were independently associated with death: 1) age ≥40 yrs, 2) anticipated death within 5 yrs, 3) nonaspiration pneumonia, 4) chest radiograph involvement >1 lobe, 5) acute respiratory failure requiring mechanical ventilation, and 6) septic shock. Based on these factors, each factor was assigned a point value, and all the factors had a point value of 1 except septic shock which had a point value of 3. The resulting risk score included three classes of increasing mortality. The main clue from this study was that whereas low-risk (point score 0–2) and high-risk (point score 6–8) patients could be confidently identified, the outcome of intermediate-risk patients was not predictable unless adjusted for evolutionary

factors independently associated with death in an additional analysis accounting for these factors only. The impact of three factors (hospital-acquired lower respiratory tract superinfections, nonspecific CAP-related complications, and sepsis-related complications) on the outcome prediction was dramatic, indicating that it is largely determined by (initially hardly predictable) complications which occur after ICU admission.

Prognostic rules for the individual hospitalized patient

Since the report by the British Thoracic Society (BTS) on CAP, indicating that inhospital outcome of the individual patient can accurately be predicted by prognostic rules including three simple clinical or laboratory parameters, there has been considerable interest in validating these rules [22, 24–27, 45, 46] (table 6). Several studies could confirm excellent operative characteristics of the original [24, 25] or a slightly modified rule [26]. The sensitivities ranged from 70–90%, and the specificities from 76–84% (table 6). More recently, two studies have failed to confirm these favourable prediction results, one in a general [27] and another in an elderly population [41].

Table 6. – Prognostic rules for the individual outcome in patients with community-acquired pneumonia and their performances

	Sens.	Spec.	PPV	NPV
Rule 1				
Derivation study [22]	88	79	19	99
Validation studies				
FARR *et al*. [24]	70	84	29	97
KARALUS *et al*. [25]*	83	80	23	99
NEILL *et al*. [26]	90	76	25	99
LIM *et al*. [27]	52	79	NR	NR
EWIG *et al*. [41]**	65	73	21	95
CONTE *et al*. [45]**	50	70	NR	NR
Rule 2				
Derivation study [22]	39	94	36	97
Validation studies				
FARR *et al*. [24]	35	89	22	94
NEILL *et al*. [26]	65	88	33	97
EWIG *et al*. [41]**	47	88	31	94
Rule 3				
Derivation study [26]	95	71	22	99
Validation study [27]	66	73	NR	NR
Rule 4				
Derivation study [28]	77	75	42	93
Validation study [41]**	47	80	21	93

Sens.: sensitivity; Spec.: specificity. PPV: positive predictive value; NPV: negative predictive value; NR: not reported. Rule 1: (original BTS-rule 1): at least two of three of the following: respiratory rate $\geq 30 \cdot min^{-1}$, diastolic blood pressure ≤ 60 mmHg, blood urea nitrogen >7 $mmol \cdot L^{-1}$; Rule 2: (original BTS-rule 2): at least two of three of the following: respiratory rate $\geq 30 \cdot min^{-1}$, diastolic blood pressure ≤ 60 mmHg, mental confusion; Rule 3: (modified BTS-rule): at least two of four of the following: respiratory rate $\geq 30 \cdot min^{-1}$, diastolic blood pressure ≤ 60 mmHg, blood urea nitrogen >7 $mmol \cdot L^{-1}$, mental confusion; Rule 4: (EWIG *et al*.): at least two of three of the following: systolic blood pressure ≤ 80 mmHg, heart rate ≥ 90 bpm, LDH ≥ 260 $U \cdot L^{-1}$. *: using rule 1 or rule 2; **: elderly population (≥ 65 yrs).

Since the majority of patients with CAP is expected to belong to the elderly population, the authors were particularly interested in the performance of the original BTS rules in these elderly patients. It was hypothesized that elevated blood urea nitrogen which is more frequently present or at least can more readily develop in the elderly would represent a confounding factor whereas mental confusion as a marker of severe sepsis would work particularly well in this frequently oligosymptomatic population. In fact, it was found that blood urea nitrogen only had a very low specificity whereas the opposite was true for mental confusion. Accordingly, the second BTS rule had the best performance as evidenced by operative indices (sensitivity 47%, specificity 88%) as well as by risk assignment of prognostic rules according to risk classes as proposed by FINE *et al*. [40].

With regards an alternative rule proposed by the authors [28], a satisfactory specificity of 80% could be confirmed but only a very limited sensitivity of 47% in this elderly population was found [41].

Looking at the performances of these rules, two issues should be pointed out. First, the predictive power of these simple rules is considerably high. This can best be explained if it is considered that these rules include parameters mainly reflecting two of the most important prognostic factors, *i.e.* acute respiratory failure (by respiratory rate $\geq 30 \cdot min^{-1}$) and severe sepsis or septic shock (by blood urea nitrogen, mental confusion, hypotension, or tachycardia). Secondly, since specificity was consistently found to be high but sensitivity to be quite variable, the true strength of these rules is their negative predictive value, *i.e.* the identification of patients who are not at risk of death from pneumonia. This value was found to exceed 90% in all validation studies published so far [24–27, 41]. Nevertheless, since these rules were derived and validated only in hospitalized patients, the applicability of these rules in triaging outpatients for hospitalization or ICU admission is not settled.

Defining severe pneumonia

Since mortality from CAP is consistently highest in patients who require admission at the ICU, ranging 25–50% [6, 19], it appears particularly important to identify such patients at highest risk for death in order to ensure intensive care as early as possible. Although since 1985 >30 series of severe CAP have been published, the only common denominator of pneumonia severity in these studies was the decision to admit the patient at the ICU in the particular hospital. Therefore, it was thought that one important way to identify objective severity criteria behind these decisions would be to determine the predictive power of such criteria for the decision to refer the patient to the ICU in an experienced tertiary care centre.

The severity criteria as suggested by the ATS guidelines for the management of adult CAP was primarily evaluated [1, 44] (table 7). With the exception of the oxygenation index, all nine remaining severity criteria were significantly associated with death. Likewise, except respiratory rate $>30 \cdot min^{-1}$ and the oxygenation index, specificity of the remaining eight severity criteria was high, ranging

Table 7. – Criteria for the definition of severe community-acquired pneumonia as suggested by the American Thoracic Society (ATS)

Baseline ("minor") criteria assessed at admission
1. Respiratory rate >30·min^{-1}
2. Severe respiratory failure ($P_{a,O_2}/F_{I,O_2}$ <250)
3. Bilateral involvement in chest radiograph
4. Involvement of >2 lobes in chest radiograph (multilobar involvement)
5. Systolic blood pressure <90 mmHg
6. Diastolic blood pressure <60 mmHg
"Major" criteria assessed at admission or during clinical course
1. Requirement for mechanical ventilation
2. Increase in the size of infiltrates by ≥50% in the presence of clinical nonresponse to treatment or deterioration (progressive infiltrates)
3. Requirement of vasopressors >4 h (septic shock)
4. Serum-creatinine ≥2 mg·dL^{-1} or increase of ≥2 mg·dL^{-1} in a patient with previous renal disease or acute renal failure requiring dialysis (acute renal failure)

Modified severity criteria as suggested by EWIG *et al*. [44] include: at least two of three of the baseline ("minor") criteria 2, 4, and 5; or at least one of two "major" criteria 1 and 3. Data as suggested by the ATS [1].

86–100%, but at the cost of a low sensitivity (range 12–52%). Similar performances were found for additional severity criteria such as mental confusion, tachycardia >125 bpm, hypercapnia and the presence of pleural effusion. However, when the recommendation of the ATS guidelines to consider ICU admission in the presence of at least one criterion out of the 10 severity criteria was applied, sensitivity was 98% but specificity only 32%. Thus, this rule would clearly result in oversensitivity and be a poor predictor of the patient at risk.

In order to develop a more balanced predictive rule of pneumonia severity, it was thought that it would be important to rearrange the ATS severity criteria according to those available after initial clinical examination (baseline parameters) and those which are assessed either at admission or during clinical course and clearly imply more severe illness (major criteria). Within both groups of parameters, those independently associated with severity were assessed by multivariate analysis, and these parameters were tested for their ability to predict pneumonia severity (table 7). The presence of two of three baseline criteria had a sensitivity of 33% and a specificity of 94%. However, if severe CAP was defined as the presence of two of three baseline or one of two major criteria, the performance was more balanced, with a sensitivity of 75%, a specificity of 94%, and a positive predictive value of 74% and a negative predictive value of 95%. Thus, it appears that those five parameters should be able to identify the patient with severe CAP quite accurately. However, this rule is pending a prospective validation in an independent patient cohort. Moreover, in addition to this rule, the clinician should remain alert to other criteria of severity, such as the presence of mental confusion and pleural effusion.

One of the most striking findings in this study was the low predictive power of parameters reflecting acute respiratory failure. However, both the respiratory rate and the oxygenation index may result in greater accuracy after the application of a defined amount of oxygen for a defined amount of supplemental oxygen, thus correcting for biases arising from the stress of the prehospitalization period.

A clear limitation of the suggested definition lies in the mix-up of baseline and potentially evolutionary criteria. An important minority of patients who do not meet severity criteria on admission may nevertheless be at high risk of developing severe CAP in the following 72 h but not receive intensive care and corresponding appropriate antimicrobial treatment. Therefore, predictors of a high risk for clinical deterioration requiring ICU treatment need to be developed which allow for the appropriate assessment of the severity of pneumonia in these patients also.

Severity assessment as part of new concepts of patient management

The assessment of severity of CAP is not only crucial for decisions about hospitalization and ICU admission but also for the selection of initial antimicrobial treatment. As outlined in the introduction, the classification into mild, moderate, and severe CAP is usually synonymous with the estimation that, as far as pneumonia severity is concerned, the patient can be treated as an outpatient or must be hospitalized or admitted to the ICU, respectively. Moreover, distinct empiric antimicrobial regimen are being recommended according to these three categories of severity based on estimations about microbial patterns associated with these categories [1–6].

More recently, new concepts have been developed which include the assessment of severity into decisions about the intensity of antimicrobial treatment and length of hospital stay. In one retrospective study, patients were classified as being low risk in case of absence of: 1) obvious reasons for continued hospitalization on the third hospital day, 2) a high-risk aetiology, and 3) a life-threatening complication within the first 3 days of hospitalization. Of 503 eligible hospitalized patients, 33% were classified as being at low risk according to these criteria and potentially suitable for early conversion to oral antimicrobial treatment [47]. In another concept, low risk patients as defined by the absence of risk factors associated with pneumonia-related morbidity or mortality are treated as outpatients with oral antibiotics whereas high risk patients are hospitalized and initially treated with intravenous antibiotics. This latter group is further subdivided into: 1) patients with primarily unstable pneumonia as defined by the presence of severe underlying comorbidity and other adverse prognostic factors; these patients are closely observed and rapidly switched to oral antibiotics and discharged in case of reaching clinical stability; and 2) patients with primarily unstable pneumonia who deteriorate and experience complicated pneumonia as defined by advanced local disease, metastatic spread of infection or systemic decompensation; these patients receive prolonged intravenous antibiotic treatment [48].

These concepts are particularly attractive because they provide a framework for the study of the optimal duration, the selection of routes and the accurate time-point to switch from intravenous to oral antimicrobial treatment in different groups at risk. Likewise, together with data provided by aforementioned studies assessing the time to

clinical stability, they may be of help in optimizing the application of supportive treatment measures and duration of hospitalization. Results of these studies are likely to change the conventional management attitudes and thereby, contribute to a substantial cost-saving in the treatment of patients with CAP.

Conclusions and future prospects

The assessment of severity plays a crucial role in the management of patients with CAP. This is true for the evaluation of the patient with LRTI, the triaging decision about hospitalization or ICU admission, and, as a consequence, selection of initial antimicrobial treatment. Severity assessment has also been increasingly applied in studies evaluating the optimal selection of routes of antimicrobial treatment application, duration of antimicrobial treatment and hospital discharge.

Factors clearly associated with adverse outcomes have been incorporated in the recommendations about severity assessment of the current guidelines for the management of adult CAP. However, beyond some clear-cut severity criteria some important topics of severity assessment remain doubtful. This is particularly true for the evaluation of patients with mild LRTI and the definition of severe CAP requiring ICU admission. Future investigations should determine whether the confirmation of infiltrates in chest radiographs of patients with mild LRTI and suspected CAP has prognostic weight important enough to render regular chest radiographs a mandatory goal of severity assessment. When attempting to improve the definitions of severe CAP, it will be important to identify predictors of imminent deterioration within the 72 h following initial empiric antimicrobial treatment.

Currently available tools for the assessment of severity of the individual patient such as prediction rules for ambulatory patients at risk for complications without obvious reasons for hospitalization [17] and for death from pneumonia in hospitalized patients [22, 24–28, 41] are simple enough to be clinically applicable. The identification of objective criteria for severe pneumonia requiring ICU admission may allow more accurate allocation of limited health care resources. Further studies will be necessary to validate and refine these or modified predictive rules in different settings. However, all predictive rules will remain far from being perfect, and the appropriate estimation of the individual risk and medical as well as nonmedical requirements will always remain a medical art.

On the other hand, risk classifications such as the scores developed by Fine *et al*. [40] are not only useful in identifying the patients at low risk who might safely be treated as outpatients but will play a major role in the evaluation of processes and outcomes of care for patients with CAP. Based on such evaluations it will be possible to define interventions aimed at reducing hospital admission rates, defining risk-adapted antimicrobial treatment regimen, reducing costs for antimicrobial treatment and supportive measures, and shortening of hospital stay. Together with these standardizations, it will be possible to recognize the true peculiarities of the particular treatment setting and to account for them appropriately. This will most likely contribute to an increased acceptance of management guidelines throughout different settings. Overall, it is to be expected that the quality of care can be substantially improved by these tools of severity assessment, and further corresponding work is anticipated in the near future.

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