

Clinical Picture and Prognostic Factors for Severe Community-Acquired Pneumonia in Adults Admitted to the Intensive Care Unit

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OBJECTIVE: In Chile very little information is available on severe community-acquired pneumonia treated in intensive care units. This study describes the clinical picture, prognostic factors, and treatment of adult patients admitted to the intensive care unit for severe community-acquired pneumonia.

PATIENTS AND METHODS: A total of 113 consecutive patients were included in this prospective, descriptive study.

RESULTS: The mean (SD) age of the 113 patients was 73 (15). Of these, 95% had associated comorbidity, and 81% were in the high-risk classes of the Pneumonia Severity Index. Etiology was identified in 31%, and the most common pathogens were *Streptococcus pneumoniae* (40%), gram negative bacilli (17%), and *Mycoplasma pneumoniae* (6%). The main complications were the need for mechanical ventilation (45%), septic shock (26%), heart failure (24%), and arrhythmias (15%). Mortality at 30 days was 16.8%, and multivariate analysis revealed the following factors to be associated with a greater risk of death: acute renal failure (odds ratio: 5.1), and glycemia above 300 mg/dL (odds ratio: 7.2).

CONCLUSIONS: The patients with severe pneumonia admitted to the intensive care unit are elderly, with a high level of comorbidity and complications, but most survive.

Key words: *Pneumonia. Community. Severe. Intensive care. Prognosis. Risk.*

Cuadro clínico y factores pronósticos de la neumonía adquirida en la comunidad grave en adultos hospitalizados en la unidad de cuidados intensivos

OBJETIVO: En Chile existe escasa información acerca de la neumonía adquirida en la comunidad de carácter grave manejada en las unidades de cuidados intensivos. En este trabajo se describen el cuadro clínico, los factores pronósticos y el tratamiento de pacientes adultos hospitalizados en la unidad de cuidados intensivos por neumonía adquirida en la comunidad grave.

PACIENTES Y MÉTODOS: Se ha realizado un estudio clínico prospectivo y descriptivo que ha incluido a 113 pacientes consecutivos.

RESULTADOS: De los 113 pacientes incluidos (edad media \pm desviación estándar: 73 \pm 15 años), el 95% tenía comorbilidad asociada y un 81% pertenecía a las categorías de alto riesgo del índice de gravedad de la neumonía (Pneumonia Severity Index). Se demostró la etiología en el 31% y los patógenos más frecuentes fueron *Streptococcus pneumoniae* (40%), bacilos gramnegativos (17%) y *Mycoplasma pneumoniae* (6%). Las principales complicaciones fueron necesidad de ventilación mecánica (45%), shock séptico (26%), insuficiencia cardíaca (24%) y arritmias (15%). La mortalidad a los 30 días fue del 16,8% y mediante un análisis multivariado se identificaron los siguientes factores asociados a mayor riesgo de muerte: insuficiencia renal aguda (odds ratio = 5,1) y glucemia mayor de 300 mg/dl (odds ratio = 7,2).

CONCLUSIONES: Los pacientes con neumonía grave ingresados en la unidad de cuidados intensivos son de edad avanzada, con una alta tasa de comorbilidad y complicaciones, pero la mayoría sobrevive.

Palabras clave: *Neumonía. Comunidad. Grave. Cuidados intensivos. Pronóstico. Riesgo.*

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Introduction

Community-acquired pneumonia (CAP) is a frequent cause of morbidity and mortality.¹ In Chile, CAP is the third leading cause of death from a specific disease and the leading cause among infectious diseases.² Between 4% and 8% of patients who require hospitalization for

CAP are in critical condition on admission and require a high level of hospital care, which may include intensive care, mechanical ventilation (MV), vasoactive drugs, invasive hemodynamic monitoring, and other support measures. Mortality among patients hospitalized for CAP ranges from 20% to 54%, and the hospital stay is usually long.³ As a result, this disease places a considerable financial burden on our health care system.

Authors in other countries have described severe pneumonia, proposed criteria for defining this entity, and identified prognostic factors to help physicians assess the severity of the patient's condition and the best initial care setting.^{4,12} To our knowledge, very little information is available on severe CAP in Chile,^{13,14} and the prognostic factors for the Chilean population have not been identified.

The objectives of the present study were to describe the clinical picture, course, and treatment of severe CAP in adult patients admitted to the intensive care unit (ICU), and to identify the predictors of mortality in this population.

Patients and Methods

The study was carried out in the Hospital Clínico de la Pontificia Universidad Católica de Chile (a 520-bed teaching hospital) between July 1, 1999 and June 30, 2001. All immunocompetent adults hospitalized for CAP were assessed prospectively and consecutively. The clinical picture and prognostic factors of this case series have already been published.¹⁵ In the present study, we analyzed the patients who were admitted to the ICU on the basis of the clinical judgment of the physicians in the emergency department or the general ward during the first 24 hours after admission. We enrolled all patients over 15 years old who fulfilled the diagnostic criteria for CAP described in the earlier study.¹⁵

Clinical Assessment on Admission

All decisions concerning ICU admission and subsequent treatment were taken by the medical team responsible for treating each patient, and the investigators did not intervene in this process in any way. The following information was recorded for all patients who fulfilled the inclusion criteria: age, sex, comorbidity, smoking status, alcohol consumption, use of antibiotics in the week prior to hospital admission, and suspicion of bronchial aspiration. The clinical picture on presentation, vital signs, and the reasons for ICU admission were also noted. On admission to the hospital, patients were assessed using the Pneumonia Severity Index, a prediction rule developed by Fine et al.¹⁶ This rule, which has been comprehensively validated, classifies patients into 5 categories according to risk of death, which ranges from 0.5% for patients in class I to 27% for those in class V. Patients were also assessed using the CURB-65 index developed by Lim et al,¹⁷ which is based on the following 5 variables: mental confusion, tachypnea of 30 or more breaths per minute, systolic blood pressure of less than 90 mm Hg or diastolic blood pressure under 60 mm Hg, age 65 years or older, and blood urea nitrogen exceeding 7 mmol/L. The

CURB-65 index groups patients into 3 categories: group 1 (patients scoring positive on 0 or 1 of the above variables), for which the mortality rate is under 2%; group 2 (2 positive variables), for which the mortality rate is 9%, and group 3 (3 or more positive variables) for which the mortality rate is 22%.

Laboratory Tests and Microbiology

The following tests were performed on admission to the hospital: complete blood count, plasma electrolytes, glucose, liver enzymes, coagulation studies, C-reactive protein, blood urea nitrogen, creatinine concentration, and arterial blood gases. The results of all the microbiological tests ordered by attending physicians were recorded. These included Gram stain and culture of expectorated sputum, 2 or more aerobic blood cultures, a respiratory virus panel (flu virus, *Parainfluenza*, respiratory syncytial virus, and *Adenovirus*), serological studies for *Mycoplasma pneumoniae*, and urinary antigen for *Legionella pneumophila* serotype 1. A bacterial pathogen was considered to be the etiologic agent when it was isolated in a good quality sputum sample (<10 epithelial cells and >25 leukocytes per low power field) if the result was matched by the Gram stain and the growth was normal or abundant, or else when the pathogen was isolated in a blood culture or in pleural fluid. Viruses were considered causative when the direct immunofluorescence test on a nasopharyngeal sample was positive. *L pneumophila* was considered to be the causative agent when a urinary antigen was detected in a urine sample, and *M pneumoniae* in the event of a single-titer immunoglobulin M assay of 1/32 or higher.

Chest Radiograph

The chest radiograph taken on hospital admission was evaluated by a radiologist who participated in the study. The radiographic pattern was classified as: *a*) alveolar infiltrate; *b*) interstitial infiltrate; or *c*) mixed pattern. In addition, the extension of the affected area was classified as unilobar or multilobar (2 or more lobes). The presence of pleural effusion, abscess, and cavitation was also recorded.

Clinical Course

The length of stay in hospital, the use and duration of MV, the prescription of vasoactive drugs, and the development of acute complications were recorded. Complications included acute renal failure (defined as creatinine ≥ 2 mg/dL in patients with no prior history of renal failure³), septic shock,¹⁸ suppurative complications (empyema, endocarditis, and meningitis), arrhythmias (atrial fibrillation, paroxysmal tachycardia), and heart failure. The initial empiric antibiotic regimen was also noted. In the patients with known etiology, the antibiotic treatment prescribed on admission was considered to have been inappropriate if the microorganism subsequently isolated was not covered or was resistant to the initial antimicrobial regimen. Finally, in-hospital and 30-day mortality were recorded in all patients.

Statistical Analysis

Results for the variables measured on a numeric scale are expressed as means (SD), and those measured on a nominal scale are expressed as percentages.

The χ^2 test was used for the univariate analysis of nominal variables, and the Mann-Whitney U test for ordinal variables, with 30-day mortality for any cause as a dependent variable. A *P* value of less than .05 was considered to be significant. The variables significantly associated with higher mortality on univariate analysis were incorporated into the stepwise multiple logistic regression analysis to identify independently predictive factors associated with a higher mortality rate. In this way, the clinical and radiographic variables that were not predictive were removed from the model. The odds ratio and 95% confidence interval (CI) were calculated for all prognostic factors.

Results

General Characteristics of the Population

Over the 2-year period, 463 patients were enrolled in the study. Of these, 113 (24.4%) were admitted to the ICU on the first day, (106 [93%] directly from the emergency department). The mean age was 73 years (range, 24-99 years), and 76% of the patients were over 65. On admission, 63% of patients had at least 1 concurrent disease, and of these 44% (n=39) had 2 or more. Table 1 shows the data recorded for this series.

Clinical Findings

The mean duration of symptoms before admission was 6 days, and the most common clinical findings are given in Table 1. The most frequent reasons for ICU admission were severe acute respiratory insufficiency defined as a ratio of PaO₂ to fraction of inspired oxygen of less than 250 (recorded in 69% of cases), shock (26%), and the need for MV (45%), or hemodynamic monitoring (18%). The mean duration of MV was 9 days (range, 1-52 days), 27% of the patients who required ventilation had chronic obstructive pulmonary disease or asthma, and mortality in this subgroup was 27.5%.

The number of patients (and the 30-day mortality) in each class of the Pneumonia Severity Index was as follows: 2 patients in class I (no deaths), 3 patients in class II (no deaths), 14 in class III (no deaths), 40 in class IV (15% mortality), and 54 in class V (24% mortality). The criteria for ICU admission defined by the American Thoracic Society in 1993¹⁹ were applied in the case of 18 of the 19 patients in classes I and II (for whom outpatient treatment or short-term hospitalization is normally recommended). The results were as follows: severe acute respiratory failure in 14 cases, need for MV in 9, multifocal pneumonia in 7, tachypnea defined as over 30 breaths per minute in 6, systolic hypotension in 4, shock in 3, altered mental status in 3, and acute renal failure in 1. Of these 18 patients, 15 met 2 or more of the aforementioned criteria.

Laboratory Results, and Microbiological and Radiographic Findings

Overall, 42% of patients had a C-reactive protein value more than 10 times the upper limit of normal

TABLE 1
History and Clinical Findings for 113 Patients With Community-Acquired Pneumonia Admitted to the Intensive Care Unit*

| | |
|--|--------------|
| Mean (SD) age, years | 73 (15) |
| Sex, men/women | 66/47 |
| History [†] | |
| Referred from a geriatric care setting | 3/113 (3) |
| Prior antibiotic treatment | 38/113 (34) |
| Current smokers [‡] | 35/100 (35) |
| Ex-smokers | 18/100 (18) |
| Comorbidity ≥ 1 | 107/113 (95) |
| Cardiovascular | 50 (44) |
| COPD/asthma | 34 (30) |
| Diabetes mellitus | 26 (23) |
| Chronic neurological disease | 17 (15) |
| Chronic renal failure | 11 (9) |
| Clinical findings [‡] | |
| Dyspnea | 94/113 (83) |
| Cough | 84/113 (74) |
| Expectoration | 73/113 (65) |
| Decreased consciousness | 46/105 (44) |
| Temperature >37.8°C | 44/110 (40) |
| RR >30 breaths/min | 58/106 (55) |
| Systolic hypotension (<90 mm Hg) | 21/110 (19) |
| Tachycardia >120 beats/min | 31/111 (28) |

*COPD indicates chronic obstructive pulmonary disease; RR, respiration rate.

[†]Results are expressed as absolute numbers with percentage between parentheses. The denominator corresponds to the number of patients in whom the condition was observed.

[‡]Current smokers and individuals who had stopped smoking less than 3 months before admission.

TABLE 2
Microbiological Findings in 113 Patients With Community-Acquired Pneumonia Admitted to the Intensive Care Unit

| Pathogens | Sputum n | Blood Cultures n | Pleural Fluid n | Serology n |
|--|-------------|------------------------|-----------------------|---------------|
| <i>Streptococcus pneumoniae</i> [*] | 5 | 9 | 1 | — |
| <i>Haemophilus influenzae</i> | 3 | 0 | 0 | — |
| <i>Escherichia coli</i> [*] | 1 | 4 | 0 | — |
| <i>Klebsiella pneumoniae</i> | 1 | 0 | 0 | — |
| <i>Staphylococcus aureus</i> | 1 | 0 | 0 | — |
| <i>Streptococcus</i> species | 0 | 1 | 0 | — |
| <i>Mycoplasma pneumoniae</i> | 0 | 0 | 0 | 3 |
| 2 pathogens | 8 | 1 | 0 | — |

*In 1 patient this pathogen was isolated in both sputum and blood culture.

(normal range, 0-0.9 mg/dL), 36% had an elevated white blood cell count (>15 000/ μ L), 8% had significant anemia (hemoglobin <10 g/dL), 33% had a creatinine concentration above 1.4 mg/dL, 45% had a blood urea nitrogen concentration over 25 mg/dL, 23% had a glucose concentration exceeding 250 mg/dL, and 8% had a low sodium concentration (<130 mEq/L).

Aerobic blood cultures were carried out in 88% of cases, Gram stain and culture of a good quality sputum sample (<10 epithelial and >25 polymorphonuclear cells per low power field) in 42%, serologic studies for *Mycoplasma* in 12%, and urinary antigen for *Legionella* in 11%. The etiologic agent was identified in 31% of

these patients (n=35). The microbiological results are shown in Table 2. The pathogens most frequently identified were *Streptococcus pneumoniae* (40%), gram negative bacilli (23%), and (*M pneumoniae* (6%). Two or more pathogens were isolated in 9 patients (26%). Four of the 15 patients (27%) who developed bacteremia died, as compared to 15 of the 84 (18%) who did not develop this complication ($P>.05$). Three of the 14 patients (21%) with pneumococcal pneumonia died, and 1 of the 15 strains (7%) isolated was penicillin resistant (minimum inhibitory concentration of 2 µg/mL). Four of the 9 patients (44%) with 2 or more pathogens (mixed etiology) died compared to 3 of the 26 patients (12%) in whom a single microorganism was isolated ($P=.06$). All 3 patients with *Pseudomonas* also had a second microorganism (pneumococcus, *Staphylococcus aureus*, and influenza A virus respectively). All of them also had comorbidity; 1 had diabetes and heart failure, another chronic obstructive pulmonary disease caused by smoking, and the third was a young woman (37 years) with severe mitochondrial myopathy who was using domiciliary MV. Two of these patients were placed on MV on admission, and the 2 who died (67%) were 84 years old.

The chest radiograph taken on admission showed an alveolar infiltrate in 95% of patients, multilobar involvement in 55%, and pleural effusion in 25%.

Antibiotic Treatment

Second and third generation cephalosporins (cefotaxime or ceftriaxone) were prescribed empirically to 95% of the patients (n=106). These cephalosporins were combined with macrolides (erythromycin or clarithromycin) in 37% of cases, with antiaerobic agents (clindamycin or metronidazole) in 32%, and with both in 8%. A second or third generation cephalosporin was prescribed as single-drug therapy to 9% of the patients. Three patients received ceftazidime, 2 vancomycin (in combination with cephalosporins), and 1 cefepime. Of the 35 cases in which etiology was established, initial empiric treatment was inappropriate in 5 patients (14%). The mortality rate in this subgroup was 40% compared to 13% among the 30 patients who received appropriate antimicrobial treatment ($P=.19$). *Pseudomonas aeruginosa* (isolated in sputum) was not initially covered in 3 of the patients who received inappropriate treatment, but once the antibiogram was available, these patients were prescribed treatment with an anti-*Pseudomonas* cephalosporin in combination with ciprofloxacin.

Complications and Length of Hospital Stay

In 67% of patients studied, at least 1 complication developed during the course of the illness. The most common were cardiac complications, such as heart failure and arrhythmias (39%), septic shock (26%), and acute renal failure (22%). The mortality rate among the patients who required vasopressor agents (shock) was 40%, compared to 8% among those who did not

develop shock ($P<.05$). Table 3 shows the frequency of the complications which developed.

The mean length of stay in hospital was 15.5 days. Hospital stay was significantly longer among patients placed on MV than among those who did not require ventilation (22 [14] as against 10 [6] days; $P<.001$).

Prognostic Factors and Mortality

Overall mortality at 30 days among the patients hospitalized for CAP was 16.8% (n=19), and the mean age of death was 78 (range, 49-90) years. All the patients who died were in risk classes IV or V of the Fine Index (94 patients in total and a mortality of 20%). The number of patients and mortality rates per group according to the CURB-65 index were as follows: 1 of the 19 patients in group 1 died (5%); 4 of the 23 patients in group 2 died (17%); 14 of the 61 patients in group 3 died (23%). Three patients (16%) died within the first 72 hours, 11 (61%) after the first week of hospitalization, and the mean interval between admission and death was 13 days.

TABLE 3
Acute Complications and 30-Day Mortality in 113 Patients With Community-Acquired Pneumonia Admitted to the Intensive Care Unit

| | Number (%) |
|--------------------------|------------|
| Complication | |
| Mechanical ventilation | 51 (45) |
| Septic shock | 30 (26) |
| Heart failure | 27 (24) |
| Arrhythmias | 13 (15) |
| Acute renal failure | 25 (22) |
| Suppurative complication | 7 (6) |
| Mortality at 30 days | 19 (16.8) |

TABLE 4
Factors Associated With 30-Day Mortality in Patients With Community-Acquired Pneumonia Admitted to the Intensive Care Unit*

| Factor | Univariate Analysis | | |
|------------------------------------|-----------------------|---------------|-------|
| | Number of Patients | Deaths, n (%) | P |
| Acute renal failure | 25 | 12 (48) | .0001 |
| Decreased consciousness | 54 | 14 (26) | .001 |
| Medical complications | 71 | 17 (24) | .011 |
| Mechanical ventilation | 51 | 14 (27) | .006 |
| Fine index >130 points | 54 | 13 (24) | .042 |
| Shock | 30 | 12 (40) | .0001 |
| Glucose >300 mg/dL | 9 | 5 (56) | .006 |
| Prothrombin time <70% [†] | 37 | 12 (32) | .012 |
| | Multivariate Analysis | | |
| | Odds Ratio | 95% CI | |
| Glucose >300 mg/dL | 7.2 | 1.2-42.7 | |
| Acute renal failure | 5.1 | 1.3-19.9 | |

*CI indicates confidence interval.

[†]Normal prothrombin time: 70%-100%.

TABLE 5
Summary of Selected Studies on Severe Community-Acquired Pneumonia*

| City or Country | No. of Patients | Age (Years) | Known Etiology (%) | Most Common Pathogens | MV (%) | Shock (%) | Mortality (%) | Predictors of Poor Outcome |
|-------------------------------------|--|-------------|--------------------|-----------------------|---------------------|-----------------|-------------------------------------|---|
| Stockholm, 1985 ⁴ | 53 [‡] | 50 | 53 | SP, MP, CP | 58 | NP | 25 | Leukocytes \leq 9.000/ μ l, immunodepression, age |
| Linköpin, 1986 ²⁷ | 30 | 50 | 50 | SP, LP, MP | 73 | 17 | 47 | FiO ₂ >0.6 on MV |
| Seville, 1990 ⁵ | 67 | 57 | 48 | SP, LP, GNB | NP | 20 | 21 | Age, debilitating disease, septic shock |
| Barcelona, 1991 ⁶ | 92 | 53 | 52 | SP, LP, MP | 61 | 24 | 22 | Rapid increase in radiographic infiltrates, shock |
| United Kingdom, 1992 ^{7,†} | 60 | 54 | 58 | SP, HI, LP | 88 | NP | 48 | NP |
| France, 1994 ^{8,†} | 132 | 58 | 72 | SP, GNB, HI | 61 | 26 | 24 | >60 years, bacteriemia, septic shock, MV, infection caused by SP or <i>Enterobacteriaceae</i> |
| Riad, 1994 ⁹ | 113 ^{‡,§} | 49 | 80 | PA, SP, SA | 55 | NP | 35 | NP |
| Barcelona, 1995 ¹⁰ | 127 ^{‡,§} | 58 | 55 | LP, SP, PA | 68 | 23 | 42 | >70 years, septic shock, APS >12, MV, bilateral radiographic involvement, infection by PA |
| Johannesburg, 1995 ¹¹ | 173 [‡] + 86 [‡] 44 [‡] and 45 [#] 69 [‡] and 48 [#] | | | SP, KP, GNB | 86 [‡] | 69 [‡] | 47 [‡] and 41 [#] | NP |
| Spain, 1996 ^{12,†} | 95 [‡] | 72 | 39 | SP, HI, GNB | 87 | 42 | 40 | Rapid increase in radiographic infiltrates, shock, APACHE >22, immunodepression, ARF |
| Singapore, 1998 ³² | 57 | 53 | 72 | BP, K sp., SA | 95 | NP | 61 | NP |
| France, 1999 ²⁶ | 472 [‡] | 63 | NP | NP | 62 | 33 | 23 | >40 years, early death within 5 days, MV, non aspiration pneumonia, radiographic involvement of >1 lobe, septic shock |
| Barcelona, 1999 ²⁸ | 89 | 65 | 53 | SP, AP, LP | 57 | 37 | 29 | Alcoholism |
| Buffalo, 2001 ²⁹ | 104 [‡] | 82 | 53 | SP, LP, SA, HI | NP | 32 | 55 | 24-hour diuresis, septic shock, multilobular involvement on chest radiograph, inappropriate antibiotic treatment |
| USA + Canada, 2002 ³⁰ | 170 | 63 | 45 | SP, HI, SA | 28-56 ^{**} | 48 | 18 | NP |
| This study in Santiago de Chile | 113 | 73 | 25 | SP, GNB, MP | 45 | 26 | 17 | Glucose >300 mg/dL, ARF |

*MV indicates mechanical ventilation; SP, *Streptococcus pneumoniae*; MP, *Mycoplasma pneumoniae*; CP, *Chlamydia pneumoniae*; NP, information not published; LP, *Legionella pneumophila*; FiO₂, fraction of inspired oxygen; GNB, gram negative bacilli; HI, *Haemophilus influenzae*; PA, *Pseudomonas aeruginosa*; SA, *Staphylococcus aureus*; APS, Acute Physiology Score; KP, *Klebsiella pneumoniae*; APACHE, Acute Physiology Score and Chronic Health Evaluation; ARF, acute renal failure; BP, *Burkholderia pseudomallei*; K sp., *Klebsiella* species; and AP, atypical pathogens.

[†]Multicenter study. [‡]Includes patients with severe immunodepression. [§]Includes patients with nosocomial pneumonia. ^{||}Results for patients with community-acquired pneumonia. ^{||}Results for patients without comorbidity. ^{**}Range of MV percentages from the 4 hospitals that participated in the study.

The variables significantly associated with greater risk of death at 30 days on univariate analysis were as follows: altered mental status, need for MV, presence of an acute complication, acute renal failure, shock, class V of the Fine index, glucose concentration above 300 mg/dL, and a prothrombin time of less than 70% (Table 4). The following variables were not statistically significant on univariate analysis: presence of symptoms for more than 7 days prior to admission, age, comorbidity (2 or more diseases), respiratory rate of 30 breaths per minute or more, hypotension (systolic blood pressure \leq 90 mm Hg), ratio of PaO₂ to fraction of inspired oxygen of less than 250, bacteremia, blood urea nitrogen above 25 mg/dL, and hyponatremia (<130 mEq/L). The following factors remained independently associated with a higher risk of death on multivariate

analysis: glucose concentration above 300 mg/dL (odds ratio, 7.2; 95% CI, 1.2-42.7), and acute renal failure (odds ratio, 5.1; 95% CI, 1.3-19.9).

Discussion

In the last 10 years, valuable information has been published on various aspects of CAP in Chile,²⁰⁻²⁴ but only scant data are available concerning patients with severe CAP admitted to ICUs.^{13,14} Some interesting findings from the present case series are discussed below.

One out of every 4 patients hospitalized for CAP was admitted to the ICU, a rate that is one of the highest in the literature. In most studies this figure varies between 3%²⁵ and 39%.⁴ The difference between studies can, in

part, be explained by the lack of any adequate definition for severe CAP, by the differences in the ways different hospitals and physicians treat this disease, by the availability of ICU beds, and by the characteristics of the population served by each particular hospital.

The mean age of the patients with severe CAP admitted to the ICU in our study was 73 years. This figure is 5% higher (4 years) than the mean age of patients with CAP admitted to our hospital,¹⁵ making it one of the oldest populations reported to date judging by the literature we analyzed (Table 5). This finding can be explained by differences between the ICU admission criteria used in each hospital, or it may reflect the increased size of the age cohort of people 65 years or over in Chile.

One surprising finding was that almost 20% of patients admitted to the ICU were in the low-risk categories of the Fine Severity Index. A review of the reasons for ICU admission revealed that only 1 of these 19 patients did not fulfill the requirements for such admission specified in the recommendations of the American Thoracic Society¹⁹ or the Sociedad Chilena de Enfermedades Respiratorias,³¹ and two thirds of these patients developed complications habitually treated in ICUs (need for MV and shock). A recent study reported that 27% of patients admitted to the ICUs of 4 North American hospitals fell into classes I to III of the Fine index.³⁰ Our finding confirms that the specificity of this index is low for predicting need for intensive care, and that other prognostic tools have similar limitations.^{3,7} Something similar occurred in our study with the CURB-65 index in that 17% of the patients belonged to the low-risk group, such that they would normally be recommended for outpatient treatment. Therefore, clinical criteria are still of fundamental importance in deciding where seriously ill patients should be treated because they take into account variables not included in the well-known prediction rules, such as whether or not the patient's overall condition warrants active intervention, the associated medical complications, the availability of beds, the preferences of patients and families, and other societal factors. On the other hand, the Fine and CURB-65 prognostic indices were shown to be useful in predicting mortality in this series of seriously ill patients; all the patients who died fell into the high-risk categories of the Fine index, and the mortality rate for those classified as group 3 by the CURB-65 index in this population was 23%, practically identical to the rate reported by Lim et al (22%).¹⁷

Other characteristics of our patients, such as the clinical picture on presentation and the etiologic agents identified, are similar to those observed in previous studies.^{6-8,11,12,27-30} In our population *S pneumoniae* was the most common pathogen, as was the case in most previous studies (Table 5). It is interesting to note that over 90% of the patients were treated with a second or third generation cephalosporin, generally in combination with macrolides or antianaerobic agents depending on whether "atypical" pathogens or

aspiration, respectively, were suspected. The use of these regimens is in accordance with the Chilean guidelines, which recommend combined therapy for patients with severe CAP.³¹ Only 9% of the patients received single-drug therapy. Although the American Thoracic Society does not recommend the use of antianaerobic agents, their prescription in Chile was recommended because at the time the guidelines were issued other agents, such as parenteral aminopenicillins with beta-lactamase inhibitors, were not available.

Another relevant finding is that the complication rate was high in the population admitted to the ICU. The most commonly reported complications were cardiovascular events, the need for VM, and shock. Other studies have also reported high, although variable, complication rates (Table 5). All of these complications give rise to the need for intensive medical and nursing care, complicated procedures that are not without risk, and supplementary treatments in addition to the basic treatment for pneumonia. Consequently, such complications prolong hospital stays and increase the financial burden on our health care system. A recent study³⁰ reported that the cost of treating patients in the ICU is 4 times that of treating patients at home (US \$21144 vs US \$5785).

It is also interesting to note that the mortality among patients with CAP admitted to the ICU (17%) was 7 times that of the adults hospitalized in a general ward¹⁵ and almost 25% higher than that of elderly patients admitted to our hospital for pneumonia. However, when we compare it to the figures reported in international studies, this rate is lower than that reported by hospitals in Spain,^{5,6,10,12,28} France,^{8,26} Sweden,^{4,27} the USA,^{29,30} South Africa,¹¹ Saudi Arabia,⁹ and Singapore.³² The reasons for these differences are not clear, but they may reflect differences in the characteristics of the populations under study, especially with respect to the initial severity of the disease and the immune status of the patients when they are referred to the ICU, or to the level of care they receive. However, the mortality rates observed in this predominantly elderly population support the thesis that age alone should not limit the decision to admit patients suffering from severe pneumonia to an ICU,¹² since most of the patients survived the CAP episode. Consequently, admission to the ICU should be considered in elderly patients with severe CAP when active management is warranted.

Univariate analysis identified 2 variables (shock and the need for MV), which have been associated with higher mortality in previous studies.^{5,6,8,10,12,26,29} However, multivariate analysis did not identify these 2 variables as independent risk factors, possibly owing to the size of the sample or to the number of events (for example, number of deaths). The logistic regression model identified 2 variables to be associated with higher mortality: glucose concentration exceeding 300 mg/dL and acute renal failure. Both of these variables have been reported previously,^{11,16} and it should be noted that they are both conditions that can be modified with medical treatment.

It has recently been shown that intensive insulin therapy reduces complications and mortality in critically ill patients with hyperglycemia,³³ which indicates the possible benefit of intervening to reduce this risk factor in patients with severe pneumonia.

Some limitations of our study must be pointed out: the number of patients was not very large, we did not record the complications caused by the treatments or procedures these patients underwent, and no standardized microbiological tests were performed to identify etiology. Finally, the focus of this study was on describing and determining prognostic factors rather than on identifying which aspects of the medical care received in the ICU was most likely to benefit patients with severe pneumonia.

In conclusion, severe cases of CAP requiring intensive care are common, the patients tend to be elderly and have multiple comorbidities, and, notwithstanding a high mortality rate and incidence of complications, most of them recover. These findings indicate that ICU admission should be considered in such cases. More regional studies are needed to define the criteria for ICU admission and to identify the most cost-effective interventions in the management of these patients.

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