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Prognosis factors and outcome of community-acquired pneumonia needing mechanical ventilation☆

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Abstract

Purpose: To evaluate the variables associated with mortality of patients with community-acquired pneumonia who require mechanical ventilation and to determine the attributable morbidity and intensive care unit (ICU) mortality of community-acquired pneumonia.

Material and Methods: Retrospective cohort study carried out in 361 ICUs from 20 countries including 124 patients who required mechanical ventilation on the first day of admission to the hospital due to acute respiratory failure secondary to severe community-acquired pneumonia. To assess the factors associated with outcome, a forward stepwise logistic regression analysis was performed, and to determine the attributable mortality of community-acquired pneumonia, a matched study design was used.

Results: We found 3 independent variables significantly associated with death in patients with community-acquired pneumonia requiring mechanical ventilation: simplified acute physiological score greater than 45 (odds ratio, 5.5 [95% confidence interval, 1.7-12.3]), shock (odds ratio, 5.7 [95% confidence interval, 1.7-10.1]), and acute renal failure (odds ratio, 3.0 [95% confidence interval,

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1.1-4.0]). There was no statistically significant difference in ICU mortality among patients with or without community-acquired pneumonia (32% vs 35%; $P = .59$).

Conclusions: Community-acquired pneumonia needing mechanical ventilation is not a disease associated with higher mortality. The main determinants of patient outcome were initial severity of illness and the development of shock and/or acute renal failure.

1. Introduction

Community-acquired pneumonia remains a common and serious illness, in spite of the availability of new antimicrobials and successful vaccines. Approximately 10% to 36% of patients with community-acquired pneumonia who need hospitalization require intensive care unit (ICU) treatment [1]. Mortality in these patients has been reported to range from 21% to 58% [2]. Prior investigations have shown that the requirement for mechanical ventilation is associated with increased mortality compared with nonventilated patients [3,4]. There are numerous studies evaluating clinical outcomes of patients with community-acquired pneumonia [2], but these studies included an overall population and the outcome of the subgroup of patients requiring mechanical ventilation has not been evaluated in detail.

The objectives of this study were to evaluate variables associated with mortality of patients with community-acquired pneumonia who require mechanical ventilation from the first day of admission to the hospital and to determine the attributable morbidity and ICU mortality of community-acquired pneumonia.

2. Materials and methods

2.1. Population study

We used the database of a prospective, multicenter, international cohort of 5183 adult patients who received mechanical ventilation for more than 12 hours from March 1, 1998, to March 31, 1998, at 361 ICUs [5]. We included in the study 124 patients (2% of overall population included in the International Study of Mechanical Ventilation) who required mechanical ventilation on the first day of admission to the hospital due to acute respiratory failure secondary to severe community-acquired pneumonia.

The following information was collected on each patient: (*a*) demographic data (sex, age, previous functional status, weight), date of admission to ICU, and initiating mechanical ventilation; (*b*) variables related to management (mode of ventilation, respiratory rate, tidal volume, applied positive end-expiratory pressure, airway pressures, need for vasoactive drugs, need for neuromuscular blockers, arterial blood gas analysis). The arterial blood gases correspond to the values obtained once daily at approximately 8:00 AM. The ventilator variables correspond to the time that the arterial blood gases were obtained. The use of neuromuscular blockers and vasoactive drugs (given for at least 3 hours in a 24-hour period) was recorded daily for a maximum of 28 days; and (*c*) the development of the following events was assessed daily during the course of mechanical ventilation for a maximum of 28 days: acute respiratory distress syndrome, barotrauma, sepsis, renal failure, hepatic failure, and coagulopathy. A patient was considered to have any of the above conditions if it was present for at least 2 consecutive days. The patients were prospectively followed up for a maximum of 28 days of mechanical ventilation and/or until discharge from the hospital and/or death.

Community-acquired pneumonia was defined as an acute infection of the pulmonary parenchyma that is associated with at least some symptoms of acute lower respiratory infection (fever or hypothermia, rigors, sweats, new cough with or without sputum production or change in color of respiratory secretions in a patient with chronic cough, chest discomfort, or the onset of dyspnea), accompanied by the presence of an acute infiltrate consistent with pneumonia on a chest radiograph, in a patient not hospitalized within 14 days before onset of symptoms [6].

2.2. Statistical analysis

Results were expressed as mean and SD, median with the interquartile range, and proportions as appropriate. We used the Student t test or Mann-Whitney U test to compare continuous variables and the χ^2 test or Fisher test to compare proportions. Significant univariate predictors for mortality were entered into a forward stepwise logistic regression analysis, with criteria entry and exit at $P < .05$ and $P < .10$, respectively. The model's goodness of fit was assessed by the method of Hosmer and Lemeshow.

To determine the attributable morbidity, defined as duration of mechanical ventilation and ICU length of stay, and attributable ICU mortality of community-acquired pneumonia, a matched study design was used, matching each patient with severe community-acquired pneumonia needing mechanical ventilation to a mechanically ventilated patient but without community-acquired pneumonia from our database. The matched variables were variables that we have reported to be associated with mortality in mechanically ventilated patients [5]: (*a*) variables present at the beginning of mechanical ventilation (age, simplified acute physiological score [SAPS II], limited activity as previous functional status); (*b*) variables related to patient

management (use of vasoactive drugs, use of neuromuscular blockers, plateau pressure >35 cm H_2O); and (*c*) complications developing over the course of mechanical ventilation (acute respiratory distress syndrome, sepsis, shock, renal failure, hepatic failure, coagulopathy, and ratio of PaO_2 to FIO_2). The variability range for matching age was ±10 years and for SAPS II was ±10 points.

3. Results

Characteristics of patients who were diagnosed with community-acquired pneumonia needing mechanical ventilation are shown in Table 1. Among these, 40 (32%) patients died during the ICU stay and 46 (37%) patients died during the hospital stay. Among surviving patients (n = 84), the destinations at hospital discharge were as follows: home (74%), nursing home (11%), acute facility (7%), and other destiny (9%).

3.1. Prognosis factors

Nonsurviving patients had a greater severity of illness at ICU admission and more shock, acute renal failure, and coagulopathy over the course of mechanical ventilation (Table 2).

Although a trend was observed toward a better evolution in patients who survived, there were no significant differences in any blood gases parameter except for ratio of PaO_2 to FIO_2. Significant differences were found in this parameter before mechanical ventilation (mean ratio of PaO_2 to FIO_2, 141 ± 71 for nonsurvivors vs 172 ± 89 for survivors; $P = .05$), at first day (mean ratio of PaO_2 to FIO_2, 144 ± 69 vs 179 ± 80; $P = .03$) and last day of mechanical ventilation (mean ratio of PaO_2 to FIO_2, 174 ± 78 vs 213 ± 74; $P = .01$), and in the degree of improving oxygenation (mean difference between last and previous value of ratio of PaO_2 to FIO_2, 34 ± 81 in nonsurvivors vs 71 ± 96 in survivors; $P = .05$).

Multivariate analysis selected 3 independent variables significantly associated with death: SAPS II greater than 45 (odds ratio, 5.5 [95% confidence interval, 1.7-12.3]), shock (odds ratio, 5.7 [95% confidence interval, 1.7-10.1]), and acute renal failure (odds ratio, 3.0 [95% confidence interval, 1.1-4.0]).

Table 1 Characteristics of patients with community-acquired pneumonia who needed mechanical ventilation (N = 124)

Age (y)	60 (18)
Female sex	42 (34)
SAPS II score (points)	46 (16)
Prior functional state (limited activity)	56 (45)
Use of vasoactive drugs	48 (38)
Use of neuromuscular blockers	17 (14)
Barotrauma	6 (5)
Acute respiratory distress syndrome	8 (6)
Sepsis	17 (14)
Shock	36 (29)
Renal failure	30 (24)
Hepatic failure	10 (8)
Coagulopathy	15 (12)
Metabolic acidosis	6 (5)
Respiratory acidosis	9 (7)

Age and SAPS II score are expressed as mean (SD) and all other values are expressed as number (%).

Table 2 Factors associated with ICU mortality in patients with community-acquired pneumonia (univariate analysis)

	Nonsurvivors (n = 40)	Survivors (n = 84)	*P*
Variables present at the beginning of mechanical ventilation			
Age (y), mean (SD)	62 (18)	58 (18)	.24
SAPS II (points), mean (SD)	57 (18)	40 (12)	<.001
Female, n (%)	29 (34.5)	13 (32.5)	.82
Prior functional state (limited activity), n (%)	18 (45%)	38 (45%)	.98
Arterial blood gases previous to mechanical ventilation, mean (SD)			
Arterial pH	7.29 (0.11)	7.29 (0.11)	.85
$PaCO_2$	51 (21)	52 (19)	.77
Ratio of PaO_2 to FIO_2	141 (71)	172 (89)	.05
Variables related with management			
Use of neuromuscular blockers, n (%)	9 (22.5)	9 (11)	.10
Ventilatory management, mean (SD)			
First day of mechanical ventilation			
Tidal volume (mL/kg)	9 (2)	9 (2)	.87
Applied PEEP (mL/kg)	5 (4)	5 (3)	.92
Plateau pressure (cm H_2O)	23 (4)	23 (5)	.98
Last day of mechanical ventilation			
Tidal volume (mL/kg)	9 (2)	9 (2)	.79
Applied PEEP (mL/kg)	6 (4)	5 (2)	.25
Plateau pressure (cm H_2O)	25 (7)	23 (3)	.10
Arterial blood gases, mean (SD)			
First day of mechanical ventilation			
Arterial pH	7.38 (0.09)	7.38 (0.09)	1.00
$PaCO_2$ (mm Hg)	39 (12)	40 (13)	.64
Ratio of PaO_2 to FIO_2	144 (69)	179 (80)	.03
Last day of mechanical ventilation			
Arterial pH	7.37 (0.10)	7.40 (0.04)	.05
$PaCO_2$ (mm Hg)	40 (9)	39 (6)	.61
Ratio of PaO_2 to FIO_2	174 (78)	213 (74)	.01
Complications developing over the course of mechanical ventilation, n (%)			
Barotrauma	3 (7)	6 (7)	1.00
Acute respiratory distress syndrome	4 (10)	4 (5)	.27
Sepsis	8 (20)	9 (11)	.16
Shock	22 (55)	14 (17)	<.001
Acute renal failure	18 (45)	12 (14)	<.001
Hepatic failure	5 (12.5)	5 (6)	.21
Coagulopathy	8 (20)	7 (8)	.08
Metabolic acidosis	3 (7.5)	3 (4)	.34

3.2. Impact on outcome

Overall, 124 patients with severe community-acquired pneumonia requiring mechanical ventilation were successfully matched to a control patient without community-acquired pneumonia. Characteristics and outcomes of cases and controls are shown in Table 3.

There was no statistically significant difference in ICU mortality among patients with or without community-acquired pneumonia needing mechanical ventilation (32% vs 35%; $P = .59$).

There were no statistically significant differences in duration of mechanical ventilation (median, 5 days [interquartile range, 3-8 days] vs 4 days [interquartile range, 2-6 days]; $P = .23$) nor in length of stay (median, 8 days [interquartile range, 4-15 days] vs 6 days [interquartile range, 4-13 days]; $P = .55$) compared with patients without community-acquired pneumonia.

Table 3 Comparison of patients with community-acquired pneumonia requiring mechanical ventilation and their matched controls

	Cases (N = 124)	Controls (N = 124)	*P*
Variables present at the beginning of mechanical ventilation			
Age (y), mean (SD)	60 (18)	59 (17)	.83
SAPS II (points), mean (SD)	46 (16)	45 (16)	.82
Prior functional state (limited activity), n (%)	56 (45)	57 (46)	.97
Variables related with management, n (%)			
Use of vasoactives	48 (39)	45 (36)	.69
Use of neuromuscular blockers	17 (14)	13 (10)	.44
Plateau pressure >35 cm H_2O	6 (5)	4 (3)	.52
Complications developing over the course of mechanical ventilation, n (%)			
Barotrauma	6 (5)	5 (4)	.76
Acute respiratory distress syndrome	8 (6)	8 (6)	1.00
Sepsis	17 (14)	17 (14)	1.00
Shock	36 (29)	37 (30)	.89
Acute renal failure	30 (24)	32 (26)	.77
Hepatic failure	10 (8)	9 (7)	.81
Coagulopathy	15 (12)	15 (12)	1.00
Metabolic acidosis	6 (5)	8 (6)	.58
Ratio of PaO_2 to FIO_2 ≤200	106 (85)	102 (83)	.68
Outcomes			
Days of mechanical ventilation, median (IQR)	5 (3-8)	4 (2-6)	.23
Length of stay in the ICU, median (IQR)	8 (4-15)	6 (4-13)	.55
ICU mortality (%)	32	35	.59

IQR indicates interquartile range.

4. Discussion

The main findings of our study were that community-acquired pneumonia requiring mechanical ventilation is not associated with increase ICU mortality and it did not prolong either the duration of mechanical ventilation or the ICU length of stay. Factors significantly associated with outcome were severity of illness at ICU admission and development of cardiovascular and renal dysfunction over the course of mechanical ventilation.

In the outpatient setting, the mortality rate of pneumonia remains in the range of 1% to 5%, but among patients with community-acquired pneumonia who require hospitalization, the mortality rate increases to 12%, and in specific populations such as those with bacteremia or patients requiring admission to ICU, mortality ranges from 21% to 58% [2,7-10]. In our series, the mortality in the ICU of patients with community-acquired pneumonia requiring mechanical ventilation was 32%, in the lower range of those previously reported [7,11,12].

Several studies have analyzed the factors associated with outcome of patients with community-acquired pneumonia [13]. These factors, analyzed in a large systematic review of the literature [2] and further studies [4,7-15], can be divided into baseline variables (male sex, age, presence of coexisting disease, living in a nursing home, underlying immunosuppression or neoplasm); severity at admission at hospital (SAPS II >10-13, decreased level of consciousness, tachypnea); factors related with the pneumonia (radiographic spread of pneumonia or bilateral pulmonary involvement, aspiration pneumonia, infection caused by aerobic gram-negative pathogens, the extent of lung injury, bacteremia, requirement of mechanical ventilation, ineffective initial antibiotic therapy); and factors related with extrapulmonary complications (hypothermia, leukopenia, sepsis, septic shock, renal failure, the number of non-pulmonary organs that failed). In our cohort of mechanically ventilated patients, the variables associated with worse outcome were severity of illness on admission at ICU, shock, and acute renal failure. Although variables related to oxygenation and pulmonary parameters were not associated with outcome, we found a trend toward a better evolution in patients who survived. In a validation study of American Thoracic Society guideline severity criteria for community-acquired pneumonia by Ewig et al [7], criteria reflecting impaired oxygenation (respiratory rate >30/min and PaO_2/FIO_2 <250 at admission) were insensitive, nonspecific, and only weakly associated with mortality from severe pneumonia. To our knowledge, there are no previous studies concerning the potential prognostic value of oxygenation and pulmonary parameters over the whole course of mechanical ventilation in patients with severe community-acquired pneumonia. Most studies have evaluated hypoxemia at presentation [12,15] or over the first 24 hours of mechanical ventilation [11]. The strengths of our study were the use of a matching procedure to examine

the morbidity and mortality attributable to community-acquired pneumonia needing mechanical ventilation. In the present study, we found a control similar to each patient with community-acquired pneumonia requiring mechanical ventilation using 12 predefined variables associated with mortality [5]. We have used data from an international multicenter database adding to the validity and generalizability of the obtained results. Our sample size was large and we only included mechanically ventilated patients, whereas most of the prior studies of severe community-acquired pneumonia had mixed populations of ventilated and nonventilated patients.

We must address several limitations of our study. First, we have only used clinical criteria to diagnose pneumonia, and therefore, it has not been ascertained the importance of other potential determinants of patient outcome such as the specific microorganism responsible and the adequacy of initial antimicrobial therapy. In this sense, although some authors have observed that identifying the etiologic agent and adjusting treatment both impact patient outcome [12,16], most studies have demonstrated that causative agent was not related with outcome [2,17]. Prior antibiotic administration and adequacy of initial antimicrobial therapy were not considered in this study. Second, in our series, we did not study, as a prognostic factor, the radiographic spread of the pneumonia at ICU admission. However, in the validation study by Ewig et al [7], the two baseline radiographic criteria (multilobar or bilateral involvement in chest radiograph) had a high specificity but remained insensitive and had low positive predictive values. These observations could be due to the fact that the correlation of severe pneumonia with the extension of infiltrates visible on chest radiograph was only moderate. Third, we only took into account limited activity as prior functional status and did not account for chronic obstructive pulmonary disease, alcoholism, diabetes mellitus, and chronic heart failure, which were shown to be related with poor outcome in previous studies [4,14]. However, some other authors did not find comorbidities to influence outcome [9].

In summary, despite the above-mentioned limitations, we have found that community-acquired pneumonia needing mechanical ventilation is not a factor associated with mortality as compared with patients on mechanical ventilation for other reasons, controlling for potential confounding variables. And, it does not prolong either duration of mechanical ventilation or ICU length of stay. We also observed that initial severity of illness and the development of shock and/or acute renal failure were main determinants of patient outcome.

Appendix A

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