medicina *intensiva*

ORIGINAL

Evolution over a 15-year period of the clinical characteristics and outcomes of critically ill patients with severe community-acquired pneumonia

J. Vallés [a,b,c,*], E. Diaz [a], I. Martín-Loeches [c,d], N. Bacelar [a], P. Saludes [a], J. Lema [a], M. Gallego [e], D. Fontanals [b,f], A. Artigas [a,b,c]

[a] *Critical Care Department, Hospital Sabadell, Corporació Sanitària Universitària Parc Taulí, Sabadell, Barcelona, Spain*
[b] *Universidad Autonoma de Barcelona, Bellaterra, Barcelona, Spain*
[c] *CIBER Enfermedades Respiratorias, Spain*
[d] *Critical Care Department, Hospital St. James, Dublin, Ireland*
[e] *Respiratory Department, Hospital Sabadell, Corporació Sanitària Universitària Parc Taulí, Sabadell, Barcelona, Spain*
[f] *Microbiology Department, Hospital Sabadell, Corporació Sanitària Universitària Parc Taulí, Sabadell, Barcelona, Spain*

Abstract

Objectives: To study the characteristics and outcomes of patients in the ICU with severe community-acquired pneumonia (SCAP) over a 15-year surveillance period.

Methods: We conducted a retrospective cohort study of episodes of SCAP, and assessed the epidemiology, etiology, treatment and outcomes of patients admitted to the ICU, comparing three periods (1999–2003, 2004–2008 and 2009–2013).

Results: A total of 458 patients were diagnosed with SCAP. The overall cumulative incidence was 37.4 episodes/1000 admissions, with a progressive increase over the three periods ($P < 0.001$). Patients fulfilling the two major IDSA/ATS criteria at admission increased from 64.2% in the first period to 82.5% in the last period ($P = 0.005$). *Streptococcus pneumoniae* was the prevalent pathogen. The incidence of bacteremia was 23.1%, and a progressive significant reduction in overall incidence was observed over the three periods ($P = 0.02$). Globally, 91% of the patients received appropriate empiric antibiotic treatment, increasing from 78.3% in the first period to 97.7% in the last period ($P < 0.001$). Combination antibiotic therapy (betalactam + macrolide or fluoroquinolone) increased significantly from the first period (61%) to the last period (81.3%) ($P < 0.001$). Global ICU mortality was 25.1%, and decreased over the three periods ($P = 0.001$).

Conclusions: Despite a progressively higher incidence and severity of SCAP in our ICU, crude ICU mortality decreased by 18%. The increased use of combined antibiotic therapy and the decreasing rates of bacteremia were associated to improved patient prognosis.

© 2015 Elsevier España, S.L.U. and SEMICYUC. All rights reserved.

 * Corresponding author.
   E-mail address: jvalles@tauli.cat (J. Vallés).

Evolución durante un período de 15 años de las características clínicas y resultados de los pacientes críticamente enfermos con neumonía comunitaria grave

Resumen

Objetivos: Estudiar las características y el pronóstico de los pacientes con neumonía grave adquirida en la comunidad ingresados en una unidad de cuidados intensivos (UCI) durante un período de 15 años.

Material y métodos: Estudio retrospectivo de una cohorte de pacientes con neumonía grave comunitaria en los que se analizó la evolución en la epidemiología, etiología, tratamiento y pronóstico durante un período de 15 años, comparando 3 períodos (1999-2003, 2004-2008 y 2009-2013).

Resultados: Un total de 458 pacientes fueron diagnosticados de neumonía. La incidencia media global durante el período estudiado fue de 37,4 episodios/1.000 ingresos, encontrándose un incremento progresivo durante los 3 períodos estudiados (p < 0,001). Los pacientes que cumplían con los 2 criterios mayores de neumonía grave de la ATS/IDSA aumentaron de un 64,2% en el primer período a un 82,5% en el último período (p = 0,005). *Streptococcus pneumoniae* fue el microorganismo más frecuente aislado. La incidencia de bacteriemia fue del 23,1%, encontrándose una reducción significativa y progresiva en la incidencia a lo largo de los 3 períodos (p = 0,02). El 91% de los pacientes recibió tratamiento antibiótico empírico apropiado, encontrándose un incremento entre el primer y el último período del 78,3% al 97,7% (p < 0,001). El tratamiento combinado (betalactámico + macrólido o quinolona) aumentó de un 61% en el primer período a un 81,3% en el último (p < 0,001). La mortalidad en la unidad de cuidados intensivos durante todo el período fue del 25,1%, encontrándose una disminución progresiva durante los 3 períodos (p = 0,001).

Conclusiones: A pesar de un incremento progresivo en la incidencia y gravedad de las neumonías ingresadas en unidad de cuidados intensivos, la mortalidad se redujo en un 18%. El incremento en la utilización de tratamiento combinado y la disminución en la incidencia de bacteriemia se asociaron a una mejoría en el pronóstico.

© 2015 Elsevier España, S.L.U. y SEMICYUC. Todos los derechos reservados.

Introduction

In the United States, community-acquired pneumonia (CAP) affects >5 million adults and accounts for >1 million hospital admissions each year due to the severity of the disease or decompensation of underlying comorbid disease.[1,2] Severe CAP (SCAP) requiring critical care affects 10–22% of these.[3,4] Morbidity and mortality in patients remain high, despite advances in critical care management and antimicrobial therapy. Mortality in those admitted in to the intensive care unit (ICU), ranges from 21% to 58%.[5–7]

Early empiric antimicrobial therapy has proven the most effective approach to decreasing mortality in patients with SCAP. Various organizations, most notably the Infectious Diseases Society of America (IDSA)/American Thoracic Society (ATS)[8] and the British Thoracic Society (BTS)[9] have published guidelines for managing CAP. Adherence to guidelines has resulted in significant benefits for patients with CAP. In addition, other strategies such as lung protective-ventilation strategy[10] and Surviving Sepsis Campaign[11] recommendations introduced in recent years have improved outcomes in patients with severe sepsis admitted in the ICU.

We hypothesized that mortality in patients admitted to the ICU with SCAP has decreased even after implementation a higher organ support demand. In the current study we aimed to analyze changes in the epidemiology of SCAP in a large ICU population during 15-years' surveillance and to determine the evolution of mortality rate and the factors associated with outcome.

Materials and methods

Study population

We conducted a retrospective cohort study of episodes of SCAP admitted to the ICU at university hospital in Spain (between January 1, 1999 and December 31, 2013).

Data abstraction

The following information was recorded using standardized methods: sex, age, alcohol use, comorbidities, initially prescribed antibiotic regimen, microbiological findings, and etiologic diagnosis. Intubation and mechanical ventilation requirements, systemic response and patient outcome were also recorded. Patients were observed until death or ICU discharge. Patients' severity at admission was determined by major criteria of IDSA/ATS score.[8]

Definitions

CAP was defined as an acute lower respiratory tract infection characterized by (1) evident acute pulmonary infiltrate compatible with pneumonia on chest radiographs, (2) confirmatory findings on clinical examination, and (3) acquisition of the infection outside of a hospital.

In accordance with criteria reported elsewhere,[4] an organism was considered to be a definitive etiologic agent if one of the following conditions were met: (1) blood cultures positive for bacterial pathogens (in the absence of an extrapulmonary source of infection); (2) pleural fluid cultures yielding a bacterial pathogen; (3) in intubated patients, significant quantitative culture growth from respiratory specimens (protected specimen brush cultures $\geq 10^3$ cfu/ml, bronchoalveolar lavage fluid cultures $\geq 10^4$ cfu/ml, or quantitative endotracheal aspirate cultures $\geq 10^6$ cfu/ml); (4) in non-intubated patients a positive expectorated sputum culture with ≤ 10 epithelial cells and ≥ 25 polymorphonuclear cells per high power field; (5) detection of *Streptococcus pneumoniae* or *Legionella* urinary antigen enzyme immunoassay. Influenza viruses were diagnosed by polymerase chain reaction (PCR) assay. Identification of *Pneumocystis jiroveci* by direct immunofluorescence or culture of *Legionella pneumophila* or *Mycobacterium tuberculosis* from any of the samples was also considered to be sufficient for a diagnosis of CAP.

Cases where two or more pathogens were detected were classified as polymicrobial infection.[4] Cases where no pathogens were detected were classified as CAP of unknown origin.

Alcoholism, chronic obstructive pulmonary disease (COPD), diabetes, and other comorbidities were diagnosed according to criteria reported elsewhere.[12] Patients were considered immunocompromised when they had primary immunodeficiency or immunodeficiency secondary to radiation treatment, use of cytotoxic drugs or steroids (daily doses of 20 mg of prednisolone or the equivalent for 2 weeks), or AIDS. Shock was defined as the need for vasopressors for ≥ 4 h after fluid replacement.

Initial empirical treatment was defined as appropriate if an antibiotic prescribed within 24 h of the first encounter with the patient matched the in vitro susceptibility of a pathogen deemed to be the likely cause of infection. Treatment decisions, including antibiotic prescriptions, were taken by attending physicians and were protocolized according to local adapted guidelines.

The ethics committee approved the study and waived the need for informed consent due to the observational nature of the study (Ethics Committee Corporació Sanitaria Universitaria Parc Taulí, 2014/675).

Data analysis

To analyze trends in SCAP, we considered the annual incidence rate and defined tree 5-year periods (1999–2003, 2004–2008, 2009–2013). We did a descriptive analysis of the data. Proportions were compared using the χ^2 test with Yates correction or Fisher's exact test, when necessary. Means were compared using Student's *t* test. Values of $P < 0.05$ were considered significant. We used backward stepwise elimination logistic-regression analysis for multivariate analyses; the dependent variable was ICU mortality and the independent variables were variables registered at ICU admission and that were associated with ICU mortality in the bivariate analysis. SPSS software (version 11.0, SPSS Inc., Chicago, IL, USA) was used for all analyses.

Results

Incidence

In the 15-year period, 458 patients were admitted to the ICU for SCAP. The cumulative incidence of patients with SCAP admitted to the ICU over the whole study period was 37.4 episodes/1000 admissions, and the incidence progressively increased over the 3 periods, from 29.8 episodes/1000 admissions in the first period, to 48.9 episodes/1000 admissions in the third period ($P < 0.001$).

Patient characteristics

Table 1 reports the clinical characteristics of patients with SCAP admitted to the ICU in the three periods. On admission to ICU, a 73% of patients fulfilled at least 1 ATS/IDSA major criterion, and we observed an increase in the incidence of mechanical ventilation over the three periods. We observed a non-significant upward trend in the incidence of septic shock over the 3 periods. The incidence of patients fulfilling the two major IDSA/ATS criteria at admission (mechanically ventilation and need for vasopressors) increased from 64.2% in the first period to 82.5% in the last period ($P < 0.01$).

Microbiologic characteristics

We observed significant variations in the etiology of SCAP over the 3 periods (Table 2). *S. pneumoniae* was the most frequent pathogen in all 3 periods, with an overall incidence of 41.7%. We observed a non-significant trend toward a progressive reduction in the incidence of *L. pneumophila* over the 3 periods and a significant increase in polymicrobial episodes and viral pneumonias in the last period. Among patients with viral pneumonia, influenza was diagnosed in 64% of the episodes, all of which occurred in the last period (2009–2013). Among polymicrobial episodes, 35.2% were co-infections of influenza and *S. pneumoniae* or *Staphylococcus aureus* and 23.5% were co-infections of *S. pneumoniae* and *Haemophilus influenzae*. The overall incidence of SCAP episodes of unknown etiology was 27.5%. The overall incidence of SCAP episodes with bacteremia was 23.1%; *S. pneumoniae* was the microorganism most frequently responsible for bacteremia in the 3 periods, accounting for 81.1% of all episodes. We observed a progressive decrease in the overall incidence of bacteremia over the 3 periods ($P = 0.02$) (Fig. 1); this decrease was primarily due to the significant decrease in the incidence of *S. pneumoniae* bacteremia.

Antibiotic therapy

Of the 332 (72.5%) patients with definitive etiology, 302 (91%) were administered appropriate empiric antibiotic

Table 1 Characteristics of the patients with severe community-acquired pneumonia.

	Total n:458	P1 n:124	P2 n:153	P3 n:181	P
Age ($\pm$ SD)	61.3 (16)	59.5 (18)	63.3(16)	60.6(16)	0.13
Male gender (%)	69.0	70.2	70.6	67	0.21
Severity					
Apache II (mean $\pm$ SD)	19.0 $\pm$ 7.9	20.8 $\pm$ 7.5	18.6 $\pm$ 8.1	18.1 $\pm$ 7.7	0.03
CURB-65 (mean $\pm$ SD)	3.0 $\pm$ 1.1	2.9 $\pm$ 1.1	3.2 $\pm$ 1.0	2.9 $\pm$ 1.1	0.01
$\geq$1 major criteria IDSA/ATS (%)	73.0	64.2	72.8	82.5	<0.01
Comorbidities (%)					
COPD	30.8	27.6	34.4	28.0	0.42
Alcoholism	14.4	18.0	11.0	14.4	0.26
Chronic renal failure	4.8	8.9	5.2	1.6	0.01
Cardiovascular disease	21.0	23.4	24.8	16.0	0.10
Cancer	15.3	12.1	15.0	17.7	0.41
Diabetes	24.1	28.5	26.8	17.1	0.04
HIV	8.1	5.6	9.2	8.8	0.50
Immunocompromised	9.6	8.9	7.2	12.2	0.29
Patients with $\geq$2 comorbidities	52.3	53.7	54	49.5	0.60
Septic shock (%)	47.2	38.2	44.8	50.0	0.54
Mechanical ventilation (%)	67.2	56.9	63.0	72.0	0.02

treatment. The proportion of patients administered appropriate empiric antibiotic treatment increased from 78.3% in the first period to 97.7% in the last period ($P < 0.001$). The use of combination antibiotic therapy (betalactam + macrolide or fluoroquinolone) also increased between the first and last periods (61% vs. 81.3%) ($P < 0.001$). Cephalosporins (87.3%), particularly ceftriaxone, were the most widely used antibiotics for treating SCAP, followed by macrolides (75.7%) and quinolones (7.2%) (Table 3). We observed a significant increase in the use of cephalosporins and azithromycin over the three periods in parallel to a decrease in the use of clarithromycin.

Mortality

Overall ICU mortality was 25.1%; ICU mortality progressively decreased over the periods from 37.9% in the first period to 19.9% in the last period ($P = 0.001$). This progressive decrease in ICU mortality over the 3 periods also held true for the subgroups of patients with bacteremia, patients with septic shock, and mechanically ventilated patients (Fig. 2). The mortality of patients with combined treatment with cephalosporin and macrolides was 25.6% and the combination with quinolones was 26.7% (P:1.00). Variables significantly associated with death in the bivariate analysis

Table 2 Distribution of etiology of severe community-acquired pneumonia over 15 years.

Pathogen (%)	Total n:458	P1 n:124	P2 n:153	P3 n:181	P
Streptococcus pneumoniae	191 (41.7)	49 (38.7)	73 (47.7)	70 (38.6)	0.18
Legionella pneumophila	29 (6.3)	13 (10.4)	8 (5.2)	8 (4.4)	0.08
Virus[a]	25 (5.4)	5 (4.0)	4 (2.6)	16 (8.8)	0.03
Pseudomonas aeruginosa	12 (2.6)	4 (3.2)	8 (5.2)	–	0.01
Staphylococcus aureus	10 (2.1)	3 (2.4)	4 (2.6)	3 (1.6)	0.80
Enterobacteriaceae	10 (2.1)	4 (3.2)	4 (2.6)	2 (1.1)	0.40
Pneumocystis jiroveci	8 (1.7)	2 (1.6)	2 (1.3)	4 (2.2)	0.80
Haemophilus influenzae	6 (1.3)	2 (1.6)	1 (0.6)	3 (1.6)	0.60
Other Gram positive	4 (0.8)	1 (0.8)	–	3 (1.6)	0.20
Miscellaneous[b]	17 (3.7)	8 (6.4)	5 (3.2)	4 (2.2)	0.10
Polymicrobial	20 (5.4)	1 (0.8)	2 (1.3)	17 (9.3)	<0.001
Unknown origin	126 (27.5)	33 (26.6)	42 (27.4)	51 (28.1)	0.9

[a] Varicella, Influenza.
[b] Chlamydophila sp., Fusobacterium sp., M. tuberculosis, Aspergillus sp., Nocardia sp.

Table 3 Antibiotic treatment over 15 years.

Antibiotic (%)	Total n:458	P1 n:124	P2 n:153	P3 n:181	P
Cephalosporins	87.3	76.6	89.5	92.8	<0.001
Clarithromycin	29.0	66.9	31.4	1.1	<0.001
Azithromycin	46.7	0.8	45.8	79.0	<0.001
Levofloxacin	6.3	1.6	10.5	6.1	0.01
Ciprofloxacin	0.9	1.6	1.3	0	0.25
Amoxicillin–clavulanic	2.2	5.6	1.3	0.6	0.008
Other[a]	35.1	27.1	33.4	39.5	<0.001

[a] Carbapenems, aminoglycosides, cotrimoxazole, antivirals, tuberculostatics.
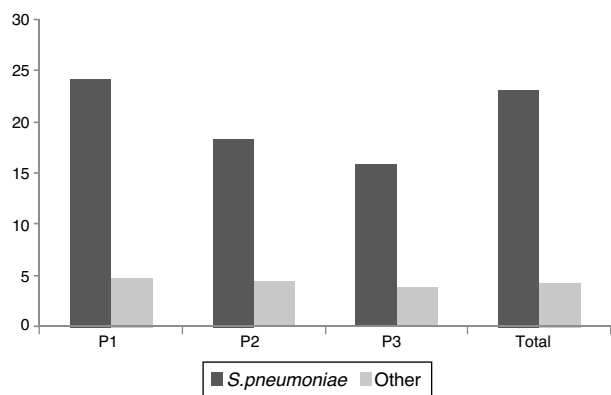P1 (1999–2003), P2 (2004–2008), P3 (2009–2013).

Table 4 Prognostic factors associated with mortality (bivariate analysis).

Variables	Patients, n (%)	Death (%)	P
Age			
<65 yrs	246 (53.7)	20.2	0.001
≥65 yrs	212 (46.3)	33.5	
Sex			
Male	316 (68.9)	26.2	0.399
Female	142 (31.1)	23.2	
Acute Physiology and Chronic Health Evaluation II Score			
≥15	301 (65.7)	31.2	0.001
<15	157 (34.3)	17.2	
Period of admission			
P1 (1999–2003)	124 (27.0)	37.9	0.001
P2 (2004–2008)	153 (33.4)	20.9	
P3 (2009–2013)	181 (39.5)	19.9	
Comorbidities			
COPD	141 (30.7)	27.7	0.415
Alcoholism	69 (15.0)	24.6	1.000
Chronic renal failure	22 (4.8)	31.8	0.455
Cardiovascular disease	96 (20.9)	26.0	0.793
Cancer	70 (15.2)	40.0	0.003
Diabetes	88 (19.2)	18.2	0.102
VIH	37 (8.0)	27.0	0.843
Immunocompromised	44 (9.6)	45.5	0.003
Bacteremia	106 (23.1)	32.1	0.073
Septic shock	216 (47.1)	31.9	0.002
Mechanical ventilation	308 (67.2)	29.9	0.001
Appropriate empiric antibiotic treatment[a]	302 (90.9)	25.5	0.009

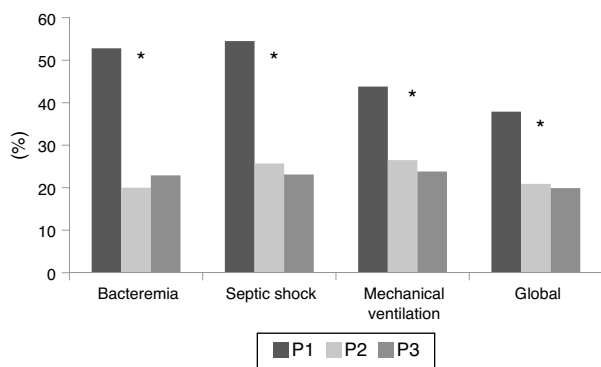[a] Only episodes with microbiologic diagnostic.

Table 5 Multivariate analysis for independent factors associated with ICU mortality.

Variables	Odds ratio	95% Confidence interval	Variables
Admission in the period 1 (1999–2003)	3.59	2.05–6.30	<0.001
Immunosuppression	2.11	0.98–4.50	0.05
Bacteremia	1.75	1.01–3.02	0.04
Mechanical ventilation	1.68	1.00–2.83	0.04
Age ≥ 65 yrs	1.03	1.01–1.04	<0.001
Appropriate empiric antibiotic treatment	0.472	0.23–0.95	0.03

P=.02 (Incidence bacteremic pneumococcal pneumonia between 3 periods)
P1 (1999-2003), P2 (2004-2008), P3 (2009-2013)

Figure 1 Incidence of bacteremic episodes over the 3 periods.

* P=.001
P1 (1999-2003), P2 (2004-2008), P3 (2009-2013)

Figure 2 Evolution of mortality over the three periods.

are shown in Table 4. In the multivariate analysis the variable associated with the highest risk of death was admission during the first period (OR 3.59, CI 2.05–6.30; *P* < 0.001). Table 5 shows further details from the multivariate analysis. Repeating the multivariate analysis, only with episodes with etiologic diagnosis, the variables selected but the model were identical, maintaining the appropriate treatment as a protective factor.

Discussion

This study provides a comprehensive picture of the clinical and microbiologic epidemiology of SCAP over 15-year periods in a large ICU population. The main findings were the progressively higher incidence of SCAP in patients admitted to ICU and the 18% reduction in crude ICU mortality.

Although the definition of SCAP remains somewhat subjective and imprecise, in practice, SCAP is often defined by respiratory and/or circulatory failure requiring admission to the ICU.[13] The IDSA/ATS Joint Guidelines list two major criteria for SCAP, septic shock and the need for mechanical ventilation, either of which is sufficient for the diagnosis.[8] Although for various reasons, such as local policies and resource availability, not all patients admitted to ICUs meet the aforementioned criteria, the patients included in the

present study had a high incidence of septic shock and need for mechanical ventilation. In fact, the incidence of patients admitted to our ICU with SCAP who had septic shock or required mechanical ventilation increased over the three periods. However, despite the increase in the incidence of shock and need for mechanical ventilation, we observed a progressive reduction in Apache II scores at admission. This reduction was attributed in part to a reduction in the incidence of preexisting comorbidities such as chronic renal failure, diabetes, and cardiovascular disease in the last period.

In recent years, hospital admissions for pneumonia have increased in the United States, Denmark, and the Netherlands.[14–17] Our study found a progressive increase in the incidence of SCAP in patients admitted to our ICU over a 15-year period (15.7% between the first and second periods and 41.7% between the second and third periods). The overall increase of the incidence of SCAP between 1999 and 2013 was 64%; these results are in line with those reported in the largest multicenter study of admissions to the ICU for CAP published in 2006 where the incidence between 1995 and 2004 rose 128%.[18] This increase in the number of patients with pneumonia admitted to ICUs could be attributed to an increase in the incidence of pneumonia patients admitted to the hospital or to an increase in the availability of ICU beds, which would allow more hospitalized patients to be admitted to the ICU. However, the number of beds in our ICU remained unchanged throughout the study period, so the increase in the number of patients with SCAP admitted to ICU is most likely due to other factors. Our results suggest that the main reason for the progressive increase in the incidence of SCAP was the increased severity of patients admitted with CAP. Indeed, the proportions of patients admitted with septic shock and of those requiring invasive mechanical ventilation increased over time (64.2% fulfilled $\geq$ 1 major criteria of ATS/IDSA at admission in the first period, 72.8% in the second period, and 82.5% in the third period; *P* < 0.01).

The most frequently isolated pathogen was *S. pneumoniae*, and there were no significant differences between the 3 periods. This finding is not surprising, as *S. pneumoniae* continues to be the leading microorganisms causing SCAP despite widespread pneumococcal vaccination programs.[8] The second most frequently isolated pathogen responsible of SCAP in our study was *L. pneumophila*. However, most of the *L. pneumophila* cases accounted in the first period and the incidence remained stable over the last decade. These findings corroborate those of a recent study about *L. pneumophila* CAP in a university hospital, which found similar stability in the incidence of ICU admission over a 15-year period.[19] Unexpectedly, the third most common cause of SCAP in our study was viral, mainly due to the increase in the incidence of influenza pneumonia in the last period. The 2009 influenza A H1N1 pandemia significantly increased the incidence of viral pneumonias and created the need for the use of rapid techniques that have improved the diagnosis of viral pneumonia. A similar increase in the incidence of viral pneumonia has been reported in different ICUs and countries since the 2009 pandemia.[20,21]

The overall incidence of bacteremia was 23%; however, we found a progressive decline in the incidence of bacteremia, largely due to the reduction in pneumococcal

bacteremia. A plausible explanation for these findings could be the widespread use of pneumococcal vaccination in general and the introduction of the 23-valent vaccine in particular. This vaccine protects against invasive pneumococcal disease, but not against less invasive infections that do not cause bacteremia as it has been suggested elsewhere.[22] A study in patients older than 65 years published in 2003[23] found that the 23-valent vaccine was effective against invasive pneumococcal disease in immunocompetent patients, but did not decrease the risk of developing any type of pneumococcal pneumonia. In our region, a pneumococcal prevention vaccination program was launched in October 1999, and a multicenter case–control study of the effectiveness of this program published in 2005 found the vaccine was 76% effective in preventing disease in immunocompetent elderly adults.[24]

Our results show a gradual change in the treatment of patients with SCAP. The use of combination antibiotic therapy increased gradually, from 61% in the first period to 81.3% in the third ($P < 0.001$). The combination of a cephalosporin with a macrolide predominated in every period, but azithromycin gradually replaced clarithromycin in the last decade. These changes were associated with a progressive increase in the effectiveness of empirical antibiotic treatment. A recent article[25] reported a similar evolution in the use of antibiotics in a study comparing prescribing practices for patients with pneumococcal SCAP between 2000 and 2013, where combination antibiotic therapy increased from 66.2% to 87.5% and the use of azithromycin progressively increased.

In our study, we also found a progressive increase in the use of other antibiotics (carbapenems, aminoglycosides, cotrimoxazole, antivirals, and tuberculostatics). This increase can be explained by two factors. First, the publication of guidelines[26] which recommended empiric antibiotic treatment in patients with healthcare-associated pneumonia in 2005 (toward the beginning of the second period) recommended empiric combination therapy with broad-spectrum antibiotics due to an increased risk of multiresistant microorganisms; second, from 2009 antiviral treatment was often included to empirically cover influenza pneumonia.

Our results show that appropriate empiric antibiotic treatment is associated with lower ICU mortality. As in other studies,[27,28] the decrease in ICU mortality can be explained in part by the increase use of combination antibiotic therapy. We also found a decrease in mortality in patients with septic shock and mechanical ventilation, corroborating the results of a recent study.[25] The decline in mortality in our study is probably also related with the progressive decrease in the incidence of bacteremia; although the influence of bacteremia on the prognosis of patients with pneumococcal pneumonia is controversial,[29] invasive pneumococcal infection has been associated with increased mortality.[30] In addition, other strategies such as lung protective-ventilation strategy[13] and Surviving Sepsis Campaign[14] recommendations introduced during the study period may be also influenced the outcome in our patients.

Our study has some limitations. First, due to the epidemiological nature of the study, antibiotic treatment, hemodynamic support and mechanical ventilation were not standardized. However, since the study was performed in a single ICU, significant variations in these aspects of patient management among physicians are unlikely. Second, the incidence of pneumococcal vaccination and pneumococcal serotypes was not recorded. Moreover, we did not distinguish between CAP and healthcare-associated pneumonia throughout the study period; nevertheless data from a recent Spanish multicenter study suggest that the prognosis among critical patients with CAP and healthcare-associated pneumonia is similar.[31]

In summary, our study shows that the incidence and mortality of SCAP have changed dramatically over the last 15 years. Despite a higher incidence of SCAP in patients admitted in the ICU, there was an 18% reduction in crude ICU mortality. This improvement in prognosis was associated with increased use of combination antibiotic therapy and a reduction in the incidence of bacteremia.

Conflict of interest

The authors do not have potential conflicts of interest with any companies/organizations whose products or services may be discussed in this article.

References

1. Kozak LJ, Owings MF, Hall MJ. National Hospital Discharge Survey: 2002 annual summary with detailed diagnosis and procedure data. Vital Health Stat. 2005;13:1–199.
2. Kung HC, Hoyert DL, Xu JQ, Murphy SL. Deaths final data for 2005: national vital statistics reports, vol. 56. Hyattsville, MD: National Center for Health Statistics; 2008.
3. Fine MJ, Auble TE, Yealy DM, Hanusa BH, Weissfeld LA, Singer DE, et al. A prediction rule to identify low-risk patients with community-acquired pneumonia. N Engl J Med. 1997;336:243–50.
4. Restrepo MI, Mortensen EM, Velez JA, Frei C, Anzueto A. A comparative study of community-acquired pneumonia patients admitted to the ward and the ICU. Chest. 2008;133:610–7.
5. Pascual FE, Matthay MA, Bachetti P, Wachter RM. Assessment of prognosis in patients with community-acquired pneumonia who require mechanical ventilation. Chest. 2000;117:503–12.
6. Wilson PA, Ferguson J. Severe community-acquired pneumonia: an Australian perspective. Intern Med J. 2005;35:699–705.
7. Fine MJ, Smith MA, Carson CA, Mutha SS, Sankey SS, Weissfeld LA, et al. Prognosis and outcomes of patients with community-acquired pneumonia: a meta-analysis. J Am Med Assoc. 1996;275:134–41.
8. Mandell LA, Wunderink RG, Anzueto A, Bartlett JG, Campbell GD, Dean NC, et al. Infectious Disease Society of America/American Thoracic Society consensus guidelines on the management of community-acquired pneumonia in adults. Clin Infect Dis. 2007;44 Suppl. 2:S27–72.
9. Lim WS, Baudouin SV, George RC, Hill AT, Jamieson C, Le Jeune I, et al. BTS guidelines for the management of community-acquired pneumonia in adults: update 2009. Thorax. 2009;64 Suppl. 3:iii1–55.
10. The Acute Respiratory Distress Syndrome Network. Ventilation with lower tidal volumes as compared with traditional tidal volumes for acute lung injury and the acute respiratory distress syndrome. N Engl J Med. 2000;342:1301–8.
11. Dellinger RP, Levy MM, Rhodes A, Annane D, Gerlach H, Opal SM, et al. Surviving sepsis campaign: international guidelines for management of severe sepsis and septic shock 2012. Intensive Care Med. 2013;39:165–228.

12. Rello J, Bodí M, Mariscal D, Navarro M, Diaz E, Gallego M, et al. Microbiological testing and outcome of patients with severe community-acquired pneumonia. Chest. 2013;123:174–80.

13. Sligl WI, Marrie TJ. Severe community-acquired pneumonia. Crit Care Clin. 2013;29:563–601.

14. Fry AM, Shay DK, Holman RC, Cums AT, Anderson LJ. Trends in hospitalizations for pneumonia among persons aged 65 years or older in the United States, 1988–2002. J Am Med Assoc. 2005;294:2712–9.

15. Hebert PL, McBean AM, Kane RL. Explaining trends in hospitalizations for pneumonia and influenza in the elderly. Med Care Res Rev. 2005;62:560–82.

16. Thomsen RW, Riis A, Norgaard M, Jacobsen J, Christensen S, McDonald CJ, et al. Rising incidence and persistently high mortality of hospitalized pneumonia: a 10-year population-based study in Denmark. J Intern Med. 2006;259:410–7.

17. Oosterheert JJ, Bonten MJ, Hak E, Lammers JW, Schneider MM, Hoepelman IM. The increase in pneumonia-related morbidity and mortality among adults in the Netherlands and possible explanations for it. Ned Tijdschr Geneeskd. 2004;148:1765–9 [in Dutch].

18. Woodhead M, Welch CA, Harrison DA, Bellingan G, Ayres JG. Community-acquired pneumonia on the intensive care unit: secondary analysis of 17,869 cases in the ICNARC Case Mix Programme Database. Crit Care. 2006;10 Suppl. 2:S1.

19. Viasus D, Di Yacovo S, García-Vidal C, et al. Community-acquired *Legionella pneumophila* pneumonia: a single-center experience with 214 hospitalized sporadic cases over 15 years. Medicine (Baltimore). 2013;92:51–60.

20. Wiemkem T, Peyrani P, Bryant K, Kelley RR, Summersgill J, Arnold F, et al. Incidence of respiratory viruses in patients with community-acquired pneumonia admitted to the intensive care unit: results from the Severe Influenza Pneumonia Surveillance (SIPS) project. Eur J Clin Microbiol Infect Dis. 2013;32:705–10.

21. Choi SH, Hong SB, Ko GB, Lee Y, Park HJ, Park SY, et al. Viral infection in patients with severe pneumonia requiring intensive care unit admission. Am J Respir Crit Care Med. 2012;186:325–32.

22. Mangtani P, Cutts F, Hall AJ. Efficacy of polysaccharide pneumococcal vaccine in adults in more developed countries: the state of the evidence. Lancet Infect Dis. 2003;3:71–8.

23. Jackson LA, Neuzil KM, Yu O, Benson P, Barlow WE, Adams AL, et al. Effectiveness of pneumococcal polysaccharide vaccine in older adults. N Engl J Med. 2003;348:1747–55.

24. Dominguez A, Salleras L, Fedson DS, Izquierdo C, Ruiz L, Ciruela P, et al. Effectiveness of pneumococcal vaccination for elderly people in Catalonia, Spain: a case–control study. Clin Infect Dis. 2005;40:1250–7.

25. Gattarello S, Borgatta B, Solé-Violán J, Vallés J, Vidaur L, Zaragoza R, et al. Decrease in mortality in severe community-acquired pneumococcal pneumonia: impact of improving antibiotic strategies (2000–2013). Chest. 2014;146:22–31.

26. American Thoracic Society, Infectious Disease Society of American. Guidelines for the management of adults with hospital-acquired, ventilator-associated, and healthcare-associated pneumonia. Am J Respir Crit Care Med. 2005;171:388–416.

27. Waterer GW, Somes GW, Wunderink RG. Monotherapy may be suboptimal for severe bacteremic pneumococcal pneumonia. Arch Intern Med. 2001;161:1837–42.

28. Baddour LM, Yu VL, Klugman KP, Feldman C, Ortqvist A, Rello J, et al. Combination antibiotic therapy lowers mortality among severely ill patients with pneumococcal bacteremia. Am J Respir Crit Care Med. 2004;170:440–4.

29. Bordón J, Peyrani P, Brock GN, Blasi F, Rello J, File T, et al. The presence of pneumococcal bacteremia does not influence clinical outcomes in patients with community-acquired pneumonia: results from the Community-Acquired Pneumonia Organization (CAPO) International Cohort study. Chest. 2008;133:618–24.

30. Musher DM, Alexandraki I, Graviss EA, Yanbeiy N, Eid A, Inderias LA, et al. Bacteremic and nonbacteremic pneumococcal pneumonia: a prospective study. Medicine (Baltimore). 2000;79:210–21.

31. Vallés J, Martin-Loeches I, Torres A, Diaz E, Seijas I, López MJ, et al. Epidemiology, antibiotic therapy and clinical outcomes of healthcare-associated pneumonia in critically ill patients: a Spanish cohort study. Intensive Care Med. 2014;40:572–81.