Arch Bronconeumol. 2015;51(11):564–570

ARCHIVOS DE BRONCONEUMOLOGIA

www.archbronconeumol.org

Original Article

Alcohol Use Disorders and Community-Acquired Pneumococcal Pneumonia: Associated Mortality, Prolonged Hospital Stay and Increased Hospital Spending☆

Miguel Gili-Miner,[a,b,*] Julio López-Méndez,[a,b] Luis Béjar-Prado,[a] Gloria Ramírez-Ramírez,[a,b] Ángel Vilches-Arenas,[a,b] José Sala-Turrens[c]

[a] Departamento de Medicina Preventiva y Salud Pública, Universidad de Sevilla, Sevilla, Spain
[b] Servicio de Medicina Preventiva y Salud Pública, Hospital Universitario Virgen Macarena, Sevilla, Spain
[c] Servicio de Documentación Clínica, Hospital Universitario Virgen Macarena, Sevilla, Spain

ARTICLE INFO

Article history:
Received 26 October 2014
Accepted 21 January 2015
Available online 20 October 2015

Keywords:
Pneumococcal pneumonia
Alcohol use disorders
Mortality
Hospital stay
Costs

ABSTRACT

Introduction: The aim of this study was to investigate the impact of alcohol use disorders (AUD) on community-acquired pneumococcal pneumonia (CAPP) admissions, in terms of in-hospital mortality, prolonged stay and increased hospital spending.
Methods: Retrospective observational study of a sample of CAPP patients from the minimum basic datasets of 87 Spanish hospitals during 2008–2010. Mortality, length of hospital stay and additional spending attributable to AUD were calculated after multivariate covariance analysis for variables such as age and sex, type of hospital, addictions and comorbidities.
Results: Among 16,202 non-elective admissions for CAPP in patients aged 18–74 years, 2685 had AUD. Patients admitted with CAPP and AUD were predominantly men with a higher prevalence of tobacco or drug use disorders and higher Charlson comorbidity index. Patients with CAPP and AUD had notably higher in-hospital mortality (50.8%; CI 95%: 44.3–54.3%), prolonged length of stay (2.3 days; CI 95%: 2.0–2.7 days) and increased costs (1869.2 €; CI 95%: 1498.6–2239.8 €).
Conclusions: According to the results of this study, AUD in CAPP patients was associated with increased in-hospital mortality, length of hospital stay and hospital spending.

Trastornos por consumo de alcohol y neumonía neumocócica adquirida en la comunidad: mortalidad atribuible, prolongación de estancias y sobrecostes hospitalarios

Palabras clave:
Neumonía neumocócica
Trastornos asociados al consumo de alcohol
Mortalidad
Estancia hospitalaria
Costes

RESUMEN

Introducción: El objetivo de este estudio es el análisis del impacto de los trastornos asociados al consumo de alcohol (TCA) en las neumonías neumocócicas adquiridas en la comunidad (NNAC), en términos de exceso de mortalidad intrahospitalaria, prolongación de estancias y sobrecostes.
Material y métodos: Estudio observacional retrospectivo de una muestra de pacientes que presentaron NNAC recogidos en los conjuntos mínimos básicos de datos de 87 hospitales españoles durante el periodo 2008-2010. Se calculó la mortalidad, la prolongación de estancias y los sobrecostes atribuibles a los TCA

☆ Please cite this article as: Gili-Miner M, López-Méndez J, Béjar-Prado L, Ramírez-Ramírez G, Vilches-Arenas Á, Sala-Turrens J. Trastornos por consumo de alcohol y neumonía neumocócica adquirida en la comunidad: mortalidad atribuible, prolongación de estancias y sobrecostes hospitalarios. Arch Bronconeumol. 2015;51:564–570.

* Corresponding author.
E-mail address: mgili@us.es (M. Gili-Miner).

1579-2129/

controlando mediante análisis multivariado de la covarianza variables como la edad y el sexo, el tipo de hospital, los trastornos adictivos y las comorbilidades.
Resultados: Se estudiaron 16.202 ingresos urgentes por NNAC de 18 a 74 años de edad, entre los cuales hubo 2.685 pacientes con TCA. Los ingresos con NNAC y TCA fueron predominantemente varones, con mayor prevalencia de trastornos por tabaco y drogas y con índices de comorbilidad de Charlson más elevados. Los pacientes con NNAC y TCA presentaron importantes excesos de mortalidad (50,8%; IC 95%: 44,3-54,3%), prolongación indebida de estancias (2,3 días; IC 95%: 2,0-2,7 días) y sobrecostes (1.869,2 €; IC 95%: 1.498,6-2.239,8 €).
Conclusiones: De acuerdo con los resultados de este estudio, los TCA en pacientes con NNAC aumentan significativamente la mortalidad, la duración de la estancia hospitalaria y sus costes.

Introduction

Mortality due to infectious diseases in Spain has been falling over the last few decades, but pneumonia remains the primary cause of death in this group (35.9%).[1] The most common type of pneumonia, and the one that causes most hospitalizations, is community-acquired pneumococcal pneumonia (CAPP),[2,3] the incidence of which remains high in Spain and the rest of Europe.[4]

Alcohol use disorders (AUDs) are a well-recognized risk factor for CAPP and have an impact on complications and outcomes of patients during admission.[5–13] AUDs increase the risk of developing sepsis during pneumonia, a complication that prolongs hospital stay, worsens prognosis[14] and increases the rate of unscheduled readmissions.[15]

We explored this problem in patients aged 18–74 years, admitted to a selected group of 87 Spanish hospitals between 2008 and 2010, and attempted to control for other confounding and interaction factors, such as age, sex, type of hospital, other addictions and comorbidities. The aim of this study was to analyze the potential influence of AUDs on mortality, prolonged stay and increased costs among patients admitted due to CAPP.

Methods

Type of Study, Sample and Participants

This was a retrospective, observational study conducted in a selected group of Spanish hospitals.

For the group to be representative of the national situation and the autonomous communities in Spain, 87 hospitals were selected from all the autonomous communities using a stepwise sampling method that took into account the Health Ministry stratification of hospitals according to size and complexity.[16]

Written or computerized clinical history data were used to code the diagnosis of each patient and the procedures he/she underwent, in accordance with the 9th Revision of the International Classification of Diseases and Causes of Death (ICD-9). Specialist personnel were responsible for coding the data and entering it in the database. These databases, known as minimum basic datasets (MBD), contain demographic information, dates of admission and discharge, type of admission and type of discharge, diagnostic codes for the main and secondary diagnoses, external causes and procedures, classified using ICD-9 codes. They also include diagnosis-related groups (DRGs), and each hospital is categorized according to size and complexity.[16]

Variables

Cases with ICD-9 code 481 in any of the MBD diagnostic codes were defined as cases of CAPP.[17,18] Scheduled admissions and patients transferred to another hospital were excluded.

Inclusion in the study was restricted to patients between 18 and 74 years of age. The Charlson comorbidity index[19] was calculated as an indicator of comorbidity, using the ICD-9 codes proposed by Quan et al.[20] for comorbidities in this index. Other comorbidities were also calculated using the codes proposed by the same authors.[20] Alcohol use disorders were defined as any problem associated with the sporadic or chronic excessive consumption of alcohol, identified in the ICD-9 codes as: alcohol dependence (303.00–303.93), alcohol abuse (305.00–305.03), alcohol-induced mental disorders (291.0–291.9), alcoholic polyneuropathy (357.5), alcoholic cardiomyopathy (425.5), alcoholic gastritis (535.30–535.31), alcoholic liver disease (571.0–571.3), excessive blood-alcohol level (790.3), and alcohol poisoning (980.0–980.9 and E860.0-E860.9). ICD-9 codes were also used for the definition of disorders associated with smoking and other addictive drugs.[21]

Hospitals were divided by size and complexity of care into 5 groups, according to the Ministry of Health, Social Services and Equality classification,[16] as required for controlling bias and calculating healthcare costs.

Data Analysis

The main objective was to determine mortality, duration of stay and hospital costs in patients with CAPP attributable to AUDs. Costs were calculated from specific hospital costs for each DRG, stratified by hospital group, according to the estimates published by the Ministry of Health for the period 2008–2010.[16]

A bivariate analysis was performed to examine the relationship between CAPP and AUDs, and age, sex, other addictive disorders and comorbidities, using the Chi-squared test (or non-parametric variants of this test) and the Student's *t*-test (or non-parametric variants). To minimize the confounding bias, a multivariate analysis of covariance was performed to determine the effect of AUDs on CAPP patients with regard to in-hospital mortality, stay and costs. The requirements of the continuous variables were verified after identifying the best-fit model, and data were adjusted for age, sex, addictions, hospital group, and patient severity (according to the Charlson index). Statistical significance was set at <.0001, due to the sample size and the multiple comparison performed. The adjusted mean of each of the dependent variables (mortality, days of hospital stay, and costs on discharge) was calculated for CAPP patients with and without AUDs, and differences were measured. The analysis was performed using the STATA statistical package, version MP 13.1.

The recommendations of the STROBE guidelines for observational studies were followed in the design, analysis and presentation of results, as applicable.

Results

Patient Characteristics

At total of 16,202 admissions for CAPP were identified: 10,635 men (65.6%) and 5567 women (34.4%). Distribution by age group

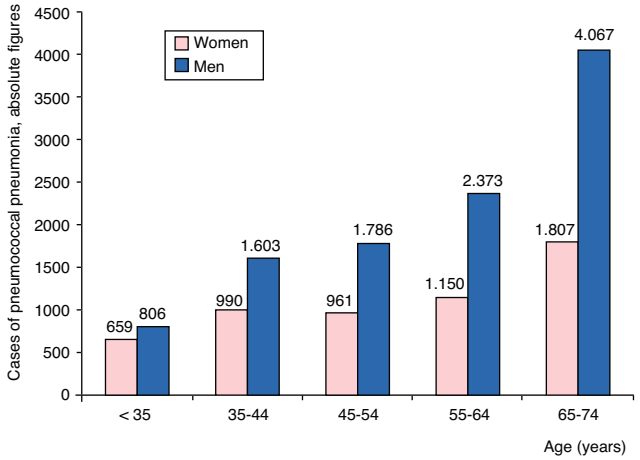

Fig. 1. Distribution of admissions for community-acquired pneumococcal pneumonia by age and sex, in absolute figures.

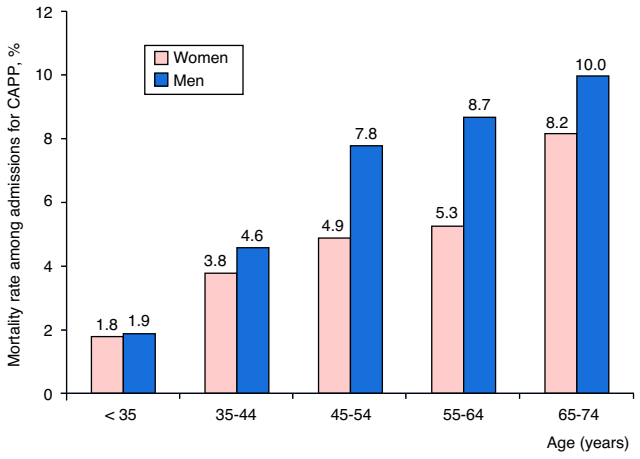

Fig. 3. Mortality rates among admissions for pneumococcal pneumonia by age and sex, in percentages.

and sex of patients admitted for CAPP are shown in Fig. 1. The number of admissions can be seen to rise progressively with age, primarily in men, until the age of 74 years.

A total of 2685 patients with CAPP had AUDs (16.6%), and differences between the sexes were notable: 2353 men (22.1%) and 332 women (6.0%). Distribution by age and sex of admissions for CAPP with AUDs is shown in Fig. 2, where it can be seen that AUDs were more common among men, mainly in the 45–54 years age group, followed by those aged 55–64, and then 35–44. The highest prevalence of AUDs among women was found in the 35–44 year age group, followed by those aged 45–54, and 55–64.

The characteristics of CAPP patients with and without AUDs are shown in Table 1. Patients with AUDs were mainly men, and had a higher rate of other addictions, mainly smoking (77.6%) and other drugs (19.4%). They also presented a higher prevalence of some of the comorbidities studied on admission, such as electrolyte disturbances, weight loss, coagulopathies, chronic lung disease, liver disease and AIDS, and a higher Charlson comorbidity index score.

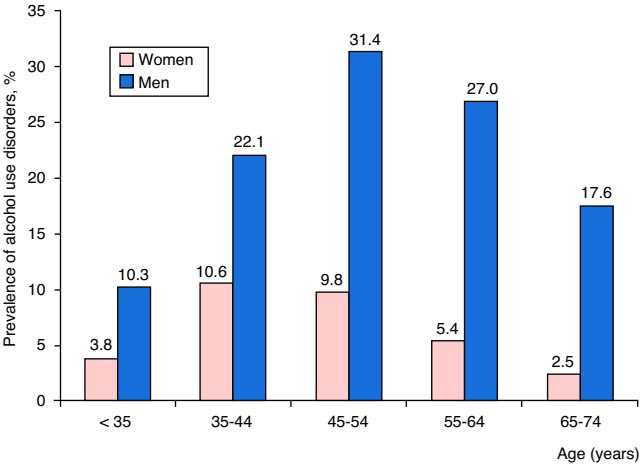

Fig. 2. Prevalence of alcohol use disorders among admissions for pneumococcal pneumonia by age and sex, in percentages.

Mortality

Distribution of mortality among CAPP patients according to age group and sex is shown in Fig. 3. Death rates were higher among men, and increased progressively with age.

The characteristics of patients admitted for CAPP who died and did not die during admission are shown in Table 2. CAPP patients who died were older (mean age, 60.5 years) and mainly men (73.3% of those who died). Some comorbidities were also found more frequently on admission, such as arrhythmias, pulmonary circulation disorders, electrolyte disturbances, weight loss, coagulopathies, congestive heart failure, cerebrovascular disease, dementia, liver disease, hemiplegia or paraplegia, kidney disease, cancer, leukemia, lymphoma and metastatic cancer, and a higher Charlson comorbidity index score.

Attributable Mortality, Prolonged Stay and Increased Costs

Results of the multivariate analysis of covariance, which included age, sex, hospital group, all addictions, and the Charlson comorbidity index, are shown in Table 3. Of the 2685 CAPP patients with AUDs, 256 died (crude mortality rate; 9.5%), compared to 892 of the 13,517 CAPP patients without AUDs (6.6%). In the multivariate model, adjusted mean mortality rates were significantly higher among CAPP admissions with AUDs (9.8% vs 6.5%), with a 3.3% mean difference, representing an excess of AUD-associated mortality of 50.8%.

The same table shows that means adjusted for hospital stay were significantly higher among CAPP admissions with AUDs (15.0 vs 12.7 days), with a mean AUD-associated extended stay of 2.3 days.

Finally, means adjusted for costs of hospital stay were significantly higher among CAPP admissions with AUDs (€10,595.50 vs €8726.30), representing an additional cost of €1869.20 for each AUD-associated CAPP.

Discussion

Pneumococcus remains the most common causative agent of community-acquired pneumonia. In the United States, however, the rate has declined, and is now only detected in 10%–15% of hospitalized cases. This reduction has been attributed to the combined influence of various factors,[22] such as widespread administration

Table 1
Characteristics of patients with community-acquired pneumococcal pneumonia with and without alcohol use disorders.

Variables	With Alcohol Use Disorders (*n*=2685) *n* (%)	Without Alcohol Use Disorders (*n*=13,517) *n* (%)	*P*[a]
Sex			
Women	332 (12.4)	5.235 (41.8)	<.0001
Men	2.353 (87.6)	8.282 (61.3)	<.0001
Age (years), mean (CI 95%[b])	55.5 (55.5–56.05)	55.8 (55.0–56.0)	.7990
Smokers	2.084 (77.6)	5.526 (40.9)	<.0001
Other drug users	522 (19.4)	1.123 (8.3)	<.0001
Comorbidities			
Obesity	117 (4.4)	823 (6.1)	.0005
Uncomplicated hypertension	493 (18.4)	3.239 (24.0)	<.0001
Complicated hypertension	98 (3.6)	694 (5.1)	.0011
Heart arrhythmias	340 (12.7)	1.849 (13.7)	.1595
Pulmonary circulation disorders	90 (3.4)	412 (3.0)	.4064
Valve disease	79 (2.9)	571 (4.2)	.0020
Iron-deficiency anemia	104 (3.9)	431 (3.2)	.0697
Post-hemorrhage anemia	5 (0.2)	65 (0.5)	.0335
Electrolyte disturbances	238 (8.9)	826 (6.1)	<.0001
Weight loss	165 (6.1)	402 (3.0)	<.0001
Hypothyroidism	44 (1.6)	435 (3.2)	<.0001
Coagulopathy	154 (5.7)	494 (3.6)	<.0001
Previous myocardial infarction	62 (2.3)	362 (2.7)	.2740
Congestive heart failure	230 (8.6)	1.101 (8.1)	.4683
Cerebrovascular disease	97 (3.6)	521 (3.8)	.5503
Dementia	23 (0.9)	163 (1.2)	.1207
Chronic lung disease	931 (34.7)	3.539 (26.2)	<.0001
Rheumatic disease	13 (0.5)	206 (1.5)	<.0001
Peptic ulcer	21 (0.8)	100 (0.7)	.8161
Mild liver disease	443 (16.5)	457 (3.4)	<.0001
Diabetes without chronic complications	371 (13.8)	1.781 (13.2)	.3710
Diabetes with chronic complications	90 (3.4)	597 (4.4)	.0124
Hemiplegia or paraplegia	19 (0.7)	152 (1.1)	.0535
Kidney disease	102 (3.8)	578 (4.3)	.2600
Moderate or severe liver disease	245 (9.1)	130 (1.0)	<.0001
Cancer, leukemia or lymphoma	302 (11.2)	1.663 (12.3)	.1260
Metastatic cancer	91 (3.4)	565 (4.2)	.0576
Aids	320 (11.9)	978 (7.2)	<.0001
Charlson index, mean (CI 95%)	2.4 (2.3–2.5)	1.7 (1.7–1.8)	<.0001

[a] *P*<.0001 considered statistically significant.
[b] CI 95%: 95% confidence intervals.

of the pneumococcal polysaccharide vaccine in adults,[23] almost universal administration of the pneumococcal conjugated vaccine in children,[24] and falling smoking rates.[25] In Spain and other European countries where these vaccines have been used less and where high smoking rates persist, pneumococcus is still responsible for the greatest proportions of community-acquired pneumonia.[4,26]

The results obtained in this study indicate that AUDs have a considerable impact on in-hospital mortality in CAPP patients, causing significantly prolonged hospital stays and generating additional costs per discharged patient. Both occasional excessive consumption of alcohol and chronic alcohol abuse or dependency syndromes cause serious disturbances in specific and non-specific immunity, generating a risk factor not only for CAPP but also for the serious complications observed in these patients.[11,14,27]

Due to size of the sample and the diversity of the hospitals in this study, our results are generalizable and need not be limited to patients from one or a few hospitals. This, to the best of our knowledge, is the first study conducted in Spain that calculates excess mortality, prolonged stay and additional costs attributable to AUDs in CAPP patients.

The major challenge in analyzing the influence of AUDs on the prognosis and other outcomes of hospitalized patients is adequate control of the confounding bias. Length of stay, costs, and in-hospital mortality differ depending on the reason for admission, the severity of the disease, comorbidities, type of hospital, and other demographic and social patient characteristics.[28] Including the hospital group in the multivariate model for controlling the confounding bias is very important, since scientific evidence has shown that quality of medical care and outcomes differ depending on hospital type, facilities and standards of care.[1,6,7,10]

Our study has several limitations. Our data were sourced exclusively from the MBDs, and no additional patient data were provided. Throughout the study, the definitions of addictive disorders, CAPP and comorbidities were used exactly as assigned by the doctors in each hospital, and coded and entered into the databases by the data managers, with no knowledge of interhospital variability. ICD-9 codes for identifying CAPP are those internationally used for studies based on hospital discharge databases, but there is no means of corroborating these diagnoses with any clinical, radiological and laboratory criteria for diagnosing CAPP that may be mentioned in the clinical records. Previous studies have found that ICD-9 code 481 is highly sensitive and highly specific for hospitalized cases of CAPP if all and not only the principal diagnostic codes are included. This is because CAPP patients are frequently admitted with sepsis, respiratory failure or other diagnoses that are coded as the principal diagnosis, and the diagnosis of CAPP is relegated to one of the secondary diagnoses.[17,18,29] To avoid this data bias, all diagnostic codes were taken into consideration in this

Table 2
Characteristics of Patients Admitted for Community-Acquired Pneumococcal Pneumonia Who Died or Did Not Die During Hospitalization.

Variables	Died (*n*=1148) *n* (%)	Did Not Die (*n*=15,054) *n* (%)	*P*[a]
Sex			
Women	306 (26.7)	5.621 (35.0)	<.0001
Men	842 (73.3)	9.793 (65.0)	.4991
Age (years), mean (CI 95%[b])	60.5 (59.8–61.2)	55.4 (55.1–55.6)	<.0001
Smoking-related disorders	410 (35.7)	7.200 (47.8)	<.0001
Alcohol-related disorders	256 (22.3)	2.429 (16.1)	<.0001
Disorders related with other drugs	95 (8.3)	1.550 (10.3)	.0289
Comorbidities			
Obesity	41 (3.6)	899 (6.0)	.0008
Uncomplicated hypertension	243 (21.2)	3.489 (23.2)	.1191
Complicated hypertension	59 (5.1)	733 (4.9)	.6823
Heart arrhythmias	234 (20.4)	1.955 (13.0)	<.0001
Pulmonary circulation disorders	61 (5.3)	441 (2.9)	<.0001
Valve diseases	40 (3.5)	610 (4.0)	.3447
Iron-deficiency anemia	23 (2.0)	512 (3.4)	.0106
Post-hemorrhagic anemia	3 (0.3)	67 (0.4)	.3602
Electrolyte disturbances	194 (16.9)	870 (5.8)	<.0001
Weight loss	67 (5.8)	500 (3.3)	<.0001
Hypothyroidism	20 (1.7)	459 (3.0)	.0117
Coagulopathy	138 (12.0)	510 (3.4)	<.0001
Prior myocardial infarction	51 (4.4)	373 (2.5)	.0001
Congestive heart failure	174 (15.2)	1.157 (7.7)	<.0001
Cerebrovascular disease	106 (9.2)	512 (3.4)	<.0001
Dementia	29 (2.5)	157 (1.0)	<.0001
Chronic lung disease	229 (19.9)	4.241 (28.2)	<.0001
Rheumatic disease	16 (1.4)	203 (1.3)	.8982
Peptic ulcer	16 (1.4)	105 (0.7)	.0083
Mild liver disease	119 (10.4)	781 (5.2)	<.0001
Diabetes without chronic complications	149 (13.0)	2.003 (13.3)	.7535
Diabetes with chronic complications	40 (3.5)	647 (4.3)	.1873
Hemiplegia or paraplegia	31 (2.7)	140 (0.9)	<.0001
Kidney disease	159 (13.9)	521 (3.5)	<.0001
Moderate or severe liver disease	89 (7.8)	286 (1.9)	<.0001
Cancer, leukemia or lymphoma	327 (28.5)	1.638 (10.9)	<.0001
Metastatic cancer	164 (14.3)	492 (3.3)	<.0001
Aids	90 (7.8)	1.208 (8.0)	.8241
Charlson index, mean (CI 95%)	3.3 (3.1–3.4)	1.7 (1.7–1.8)	<.0001

[a] *P*<.0001 considered statistically significant.
[b] CI 95%: 95% confidence intervals.

Table 3
Death During Hospitalization, Prolongation of Stay and Additional Costs Attributable to Alcohol Use Disorders in Patients With Community-Acquired Pneumococcal Pneumonia.[a]

	Adjusted Mean in Patients Without AUD	Adjusted Mean in Patients With AUD	Differences in Means Attributable to AUD	CI 95% of Excess of Means Attributable to AUDs	*P*
Adjusted mortality rate (%)	6.5	9.8	3.3 (50.8% attributable excess mortality)	2.7–3.8 (attributable excess mortality: 44.3–54.3%)	<.0001
Adjusted stays (days)	12.7	15.0	2.3	2.0–2.7	<.0001
Adjusted costs (€)	8726.3	10,595.5	1869.2	1498.6–2239.8	<.0001

[a] Multivariate analysis of covariance adjusted for age, sex, hospital group, smoking-related disorders, drug-related disorders and Charlson comorbidity index.

study, not only the principal diagnosis. Moreover, patients with programmed admission were excluded to reduce as far as possible the inclusion of cases with possibly nosocomial pneumococcal pneumonia.

Databases such as MBDs also have notable advantages. The data collected is usually entered in nearly all hospital discharge records. As all cases are included, quite accurate estimates can be made on incidence, prevalence, comorbidities, complications, and mortality of the diseases seen.[9,30,31] These data can be analyzed retrospectively, unlike other designs that need prospective data collection. Data can be collected relatively quickly and easily over long periods and from a large number of patients, as was the case in our study, and such systematic collection considerably reduces costs. In these studies, less selection bias may be

generated than in studies in which patients or their legal representatives may refuse to provide written informed consent to participate. Another considerable advantage lies in the availability of defined costs for each DRG stratified by hospital group and year, which facilitates the calculation of excess costs due to CAPP and AUDs.

A consensus document produced by several Spanish scientific societies recommends anti-pneumococcal vaccination in adults with underlying disease, including patients with AUDs.[32] This recommendation should be following in all care settings, including hospital departments in which patients with AUDs are identified.

The results of this study are a reminder that the diagnosis of alcohol, tobacco and drug abuse and the introduction of therapy should be one of the main therapeutic objectives prior to discharge of CAPP patients. Investigating the alcohol and drug use and smoking habit of each patient is the ethical and professional duty of each physician. Strategies such as a brief talk on the risks of alcohol, smoking and drugs, and a note in the discharge report advising the primary care physician of the problem in case the patient needs to be referred to specialized detoxification units, have been shown to be effective[33–36] in preventing complications and readmissions. Reducing the number of admissions and readmissions attributable to these disorders would help to reduce the costs of sick leave from work and hospital stays, increase the availability of beds in hospitals and reduce the risk of death. Each case of CAPP associated with alcohol, smoking or drug addiction disorders that is avoided also reduces the overall burden borne by these patients and their families.

Conclusions

In patients admitted for CAPP, AUDs account for an excess in-hospital mortality of 50.8%, prolongation of stay of 2.3 days, and excess costs of €1869.20.

Funding

This study was funded by: (a) the Government Delegation for the National Drug Plan. Ministry of Health, Social Services and Equality (Grant No. 2009I017, Project G41825811), and (b) Subsidies for Funding Biomedical and Health Science Research in Andalusia for 2013. Department of Health and Social Affairs of the Government of Andalusia (PI-0271-2013).

Authors' Contribution

All authors are equally contributed to the study design, data analysis and interpretation, drafting and review of the article and approval of final version.

Conflict of Interests

The authors state that they had no conflict of interests.

References

1. López-Cuadrado T, Llácer A, Palmera-Suárez R, Gómez-Barroso D, Savulescu C, González-Yuste P, et al. Trends in infectious disease mortality rates, Spain, 1980–2011. Emerg Infect Dis. 2014;20:783–9.
2. Gil A, San Martín M, Carrasco P, González A. Epidemiology of pneumonia hospitalizations in Spain, 1995–1998. J Infect. 2002;44:84–7.
3. Menendez R, Torres A, Aspa J, Capelastegui A, Prat C, Rodríguez de Castro F. Neumonía adquirida en la comunidad. Nueva normativa de la Sociedad Española de Neumología y Cirugía Torácica (SEPAR). Arch Bronconeumol. 2010;46:543–58.
4. Rozenbaum MH, Pechlivanoglou P, van der Werf TS, Lo-Ten-Foe JR, Postma MJ, Hak E. The role of *Streptococcus pneumoniae* in community-acquired pneumonia among adults in Europe: a meta-analysis. Eur J Clin Microbiol Infect Dis. 2013;32:305–16.
5. Burman LA, Norrby R, Trollfors B. Invasive pneumococcal infections: incidence, predisposing factors and prognosis. Rev Infect Dis. 1985;7:133–42.
6. Fernandez-Sola J, Junque A, Estruch R, Monforte R, Torres A, Urbano-Márquez A. High alcohol intake as a risk and prognostic factor for community-acquired pneumonia. Arch Intern Med. 1995;155:1649–54.
7. Pastor P, Medley F, Murphy TV. Invasive pneumococcal disease in Dallas County, Texas: results from population-based surveillance in 1995. Clin Infect Dis. 1998;26:590–5.
8. Ruiz M, Ewig S, Marcos MA, Martinez JA, Arancibia F, Mensa J, et al. Etiology of community-acquired pneumonia: impact of age, comorbidity, and severity. Am J Respir Crit Care Med. 1999;160:397–405.
9. Musher DM, Alexandraki I, Graviss EA, Yanbely E, Eid A, Inderias LA, et al. Bacteremic and nonbacteremic pneumococcal pneumonia: a prospective study. Medicine (Baltimore). 2000;79:210–21.
10. Kyaw MH, Rose CE, Fry AM, Singleton JA, Moore Z, Zell ER, et al. The influence of chronic illnesses on the incidence of invasive pneumococcal disease in adults. J Infect Dis. 2005;192:377–86.
11. Samokhvalov AV, Irving HM, Rehm J. Alcohol consumption as a risk factor for pneumonia: a systematic review and meta-analysis. Epidemiol Infect. 2010;138:1789–95.
12. Bello S, Menéndez R, Torres A, Reyes S, Zalacain R, Capelastegui A, et al. Tobacco smoking increases the risk for death from pneumococcal pneumonia. Chest. 2014;146:1029–37.
13. Grau I, Ardanuy C, Calatayud L, Schulze MH, Liñares J, Pallares R. Smoking and alcohol abuse are the most preventable risk factors for invasive pneumonia and other pneumococcal infections. Int J Infect Dis. 2014;25:59–64.
14. Moss M. Epidemiology of sepsis: race, sex, and chronic alcohol abuse. Clin Infect Dis. 2005;41:S490–7.
15. Mufson MA, Hao JB, Stanek RJ, Norton NB. Clinical features of patients with recurrent invasive *Streptococcus pneumoniae* disease. Am J Med Sci. 2012;343:303–9.
16. Ministerio de Sanidad, Servicios Sociales e Igualdad. Registro de Altas de los Hospitales Generales del Sistema Nacional de Salud. CMBD. Norma Estatal; 2012. Available in: http://www.msssi.gob.es/estadEstudios/estadisticas/cmbd.htm [consulted 12.07.14].
17. Lindenauer PK, Lagu T, Shieh MS, Pekow PS, Rothberg MB. Association of diagnostic coding with trends in hospitalizations and mortality of patients with pneumonia, 2003–2009. JAMA. 2012;307:1405–13.
18. Gil-Prieto R, García-García L, Álvaro-Meca A, Méndez C, García A, Gil de Miguel A. The burden of hospitalisations for community-acquired pneumonia (CAP) and pneumococcal pneumonia in adults in Spain (2003–2007). Vaccine. 2011;29:412–6.
19. Charlson ME, Pompei P, Ales KL, McKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. J Chronic Dis. 1987;40:373–83.
20. Quan H, Sundararajan V, Halfon P, Fong A, Burnand B, Luthi JC, et al. Coding algorithms for defining comorbidities in ICD-9-CM and ICD-10 administrative data. Med Care. 2005;43:1130–9.
21. Gili-Miner M, Bejar-Prado L, Gili-Ortiz E, Ramírez-Ramírez G, López-Méndez J, López-Millán JM, et al. Alcohol use disorders among surgical patients: unplanned 30-days readmissions, length of hospital stay, excessive costs and mortality. Drug Alcohol Depend. 2014;137:55–61.
22. Musher DM, Thorner AR. Community-acquired pneumonia. N Engl J Med. 2014;371:1619–28.
23. Moberley S, Holden J, Tatham DP, Andrews RM. Vaccines for preventing pneumococcal infection in adults. CDS Rev. 2013:CD000422.
24. Griffin MR, Zhu Y, Moore MR, Whitney CG, Grijalva CG. U.S. hospitalizations for pneumonia after a decade of pneumococcal vaccination. N Engl J Med. 2013;369:155–63.
25. Current cigarette smoking among adults—United States, 2011. MMWR Morb Mortal Wkly Rep. 2012;61:889–94.
26. Huijts SM, Pride MW, Vos JM, Jansen KU, Webber C, Gruber W, et al. Diagnostic accuracy of a serotype-specific antigen test in community-acquired pneumonia. Eur Respir J. 2013;42:1283–90.
27. Szabo G, Mandrekar P. A recent perspective on alcohol, immunity, and host defense. Alcohol Clin Exp Res. 2009;33:220–32.
28. Iezzoni LI. Dimensions of risk. In: Iezzoni LI, editor. Risk adjustment for measuring health outcomes. 2nd ed. Chicago, IL: Health Administration Press; 1997. p. 43–168.
29. Gil A, Gil R, Oyagüez I, Carrasco P, González A. Hospitalisation by pneumonia and influenza in the 50–64 year old population in Spain (1999–2002). Hum Vaccine. 2006;2:181–4.
30. Powell AE, Davies HTO, Thomson RG. Using routine comparative data to assess the quality of healthcare: understanding and avoiding common pitfalls. Qual Saf Health Care. 2003;12:122–8.
31. Needham DM, Scales DC, Lapaucis A, Pronovost PJ. A systematic review of the Charlson comorbidity index using Canadian administrative databases: a perspective on risk adjustment in critical care research. J Crit Care. 2005;20:12–9.

32. Picazo JJ, González-Romo F, García A, Pérez-Trallero E, Gil P, de la Cámara R, et al. Consenso sobre la vacunación anti-neumocócica en el adulto con patología de base. Rev Esp Quimioter. 2013;26:232–52.
33. Rehm J, Roerecke M. Reduction of drinking in problem drinkers and all-cause mortality. Alcohol Alcohol. 2013;48:509–13.
34. Villalbí JR, Bosque M, Gili M, Espelt A, Brugal T. Políticas para prevenir los daños causados por el alcohol. Rev Esp Salud Publica. 2014;88:515–28.
35. Rigotti NA. Treatment of tobacco use and dependence. N Engl J Med. 2002;346:506–12.
36. Coleman T. ABC of smoking cessation. Use of simple advice and behavioural support. BMJ. 2004;328:397–9.