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Decreasing incidence and mortality among hospitalized patients suffering a ventilator-associated pneumonia

Analysis of the Spanish national hospital discharge database from 2010 to 2014

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Abstract

The aim of this study was to describe trends in the incidence and outcomes of ventilator-associated pneumonia (VAP) among hospitalized patients in Spain (2010–2014).

This is a retrospective study using the Spanish national hospital discharge database from year 2010 to 2014. We selected all hospital admissions that had an ICD-9-CM code: 997.31 for VAP in any diagnosis position. We analyzed incidence, sociodemographic and clinical characteristics, procedures, pathogen isolations, and hospital outcomes.

We identified 9336 admissions with patients suffering a VAP. Incidence rates of VAP decreased significantly over time (from 41.7 cases/100,000 inhabitants in 2010 to 40.55 in 2014). The mean Charlson comorbidity index (CCI) was 1.08 ± 0.98 and it did not change significantly during the study period. The most frequent causative agent was *Pseudomonas* and there were not significant differences in the isolation of this microorganism over time. Time trend analyses showed a significant decrease in in-hospital mortality (IHM), from 35.74% in 2010 to 32.81% in 2014. Factor associated with higher IHM included male sex, older age, higher CCI, vein or artery occlusion, pulmonary disease, cancer, undergone surgery, emergency room admission, and readmission.

This study shows that the incidence of VAP among hospitalized patients has decreased in Spain from 2010 to 2014. The IHM has also decreased over the study period. Further investigations are needed to improve the prevention and control of VAP.

Abbreviations: AIDS = acquired immunodeficiency syndrome, CCI = Charlson comorbidity index, COPD = chronic obstructive pulmonary disease, ICD-9-CM = International Classification of Diseases-Ninth Revision, Clinical Modification, IHM = in-hospital mortality, LOHS = length of hospital stay, PA = *Pseudomonas aeruginosa*, SNHDD = Spanish National Hospital Discharge Database, SOFA = Sequential Organ Failure Assessment, VAP = ventilator-associated pneumonia.

Keywords: administrative database, burden of VAP, incidence rate, mortality, ventilator-associated pneumonia

1. Introduction

Ventilator-associated pneumonia (VAP) is a type of nosocomial pneumonia that occurs in patients who receive more than 48 hours of mechanical ventilation. It is associated with mortality.[1]

Over the last years, much improvement has been achieved in understanding the underlying causes and control methods for VAP; however, these infections are still a very frequent health care associated complication.[2]

Even if several reports have shown that the incidence of VAP may be decreasing, other studies do not reach this conclusion indicating that the rate is stable over time.[3–5]

The evidence shows that VAP results in a significant increment in resource consumption and in patients requiring excess days of hospitalization. Thus, occurrence of VAP increases health system costs.[6,7]

Mortality associated with VAP has been reported to range from 33% to 50%. This rate is variable and relies heavily on the underlying medical illness.[8] However, the attributable risk of death has decreased over time, and recently, it has been estimated at 9% to 13%.[9,10] In any case, the incidence, outcomes, and mortality of VAP could vary due to several factors, including the study population, time of onset, etiologic organisms, and adequacy of antibiotic therapy.[11]

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Despite the significant impact of this disease, studies conducted on the trends of epidemiology of VAP are scarce.[12–15] Unfortunately, the impact of VAP has not been previously determined for the Spanish health care system. Administrative data could be used as primary case-finding methods for this condition.[16] A better understanding of the burden of VAP may help in reducing the incidence and improving patients' outcomes.

Our objectives were to analyze trends in the incidence, clinical characteristics, and outcomes of VAP in Spain from 2010 to 2014 using the Spanish National Hospital Discharge Database (SNHDD).

2. Methods

We conducted an observational retrospective study using the SNHDD.[17] The SNHDD includes information on the sex, age, dates of admission and discharge, up to 14 discharge diagnoses, and up to 20 procedures performed during the hospitalization. The study was conducted with all data included in the SNHDD from January 1, 2010, to December 31, 2014 (5 complete years).

The criteria for diseases and procedures were defined according to the International Classification of Diseases-Ninth Revision, Clinical Modification (ICD-9-CM), which is used in the Spanish SNHDD. We selected admissions for patients with a diagnosis of VAP (ICD-9-CM code: 997.31) in any position.

The Charlson comorbidity index (CCI) was used to assess the clinical characteristics of the patients.[18] We divided patients into 3 categories: low index, which corresponds to patients with no previously recorded disease; medium index, patients with 1 disease category; and high index, patients with 2 or more disease categories.

Irrespectively of the position at the diagnoses coding list, we retrieved data about comorbid specific conditions such as acute myocardial infarction, congestive heart failure, vascular disease, cerebrovascular disease, hemiplegia or paraplegia, dementia, chronic obstructive pulmonary disease (COPD), rheumatoid disease, peptic ulcer, liver disease, renal disease, diabetes, any type of malignancy, metastatic cancer, and acquired immunodeficiency syndrome (AIDS) using the enhanced ICD-9-CM. Furthermore, we identified the following as primary diagnosis: cranial hemorrhage, heart disease, vein or artery occlusion, cranial or spine fracture, pulmonary disease, or nonspecified pneumonia and cancer using the specific ICD-9 codes. We analyzed organ failures, procedures, and pneumonia pathogens documented during hospitalizations for VAP using the same source (see Table 1, Supplemental Content, http://links.lww.com/MD/B815).[19] According to the SNHDD methodology, only those pathogens that are laboratory confirmed can be included in the discharge report.[17] For study purpose, we grouped all species associated with rising IHM in a new variable named "All species that increased IHM." Hospital outcome variables included emergency room admission, readmission (if the patient had been discharged in the previous 30 days), and the in-hospital mortality (IHM).

2.1. Statistical analysis

In order to assess time trends, the incidence rates of hospitalizations with VAP were calculated per 100,000 inhabitants. The denominators were the population, reported on December 31 of each year, according to the Spanish National Institute of Statistics.[20]

We estimated the proportion of VAP among mechanically ventilated patients dividing the number of VAP by the total number of hospitalized patient who received invasive mechanical ventilation (ICD MD codes 96.7x in any procedure field) each year.

Variables are described as means with standard deviations or as proportions. Bivariate comparisons were done with Student *t* test, Kruskall–Wallis test, analysis of variance (ANOVA), and χ^2 test.

Multivariable methods include Poisson regression (incidence) or logistic regression (IHM). The detailed description of the methods can be found elsewhere.[19]

The software used for bivariate and multivariable analysis was Stata (Stata, College Station, TX). Statistical significance was set at $P < .05$ (2-tailed).

2.2. Ethical aspects

Approval by an ethics committee was not necessary according to the Spanish law. To warranty patient anonymity, the database was provided to us by the Ministry of Health after all patient identifiers were deleted. In accordance with the Spanish legislation, informed consent was not necessary.

3. Results

From 2010 to 2014, we identified a total of 9336 admissions with patients suffering a VAP in Spain. Table 1 summarizes the sociodemographic and clinical characteristics of patients included in the study. The mean age was 58.3 ± 18.31 years and there were a predominance of males, without significant changes in age or sex over time. Incidence decreased significantly, from 41.7 cases per 100,000 inhabitants in 2004 to 40.55 in 2014.

As can be seen in Table 1, the proportion of VAP among mechanically ventilated patients remained stable along the study period with figures around 4%.

The mean CCI index was 1.05 ± 0.98 and it did not change significantly during the study period. The most frequent comorbidities were as follows: cerebrovascular disease (21.09%), congestive heart failure (13.7%), COPD (12.14%), and diabetes (10.59%).

The most common primary diagnosis was cranial hemorrhage (15.19%), followed by heart disease (11.51%), cranial or spine fracture (7.18%), cancer (5.81%), and pulmonary disease or pneumonia (5.21%). We did not find significant variations in the prevalence of these conditions over time.

Procedures, hospital outcomes, acute organ failures, and pathogen isolations of patients hospitalized with VAP are summarized in Table 2. We found an increase in the use of bronchoscopies over time, from 12.74% in 2010 to 16.69% in 2014 ($P < .05$). However, the use of other procedures, such as the thoracentesis or the pleural drainage tube, did not change significantly during the study period.

We observed a significant decrease in the percentage of patients who had undergone surgery, from 77.17% in 2010 to 73.62% in 2014. However, we did not detect significant differences in the prevalence of pressure ulcers, septic shock, emergency room admissions, and readmissions (Table 2).

The mean number of acute organ failures significantly increased during the study period, from 1.24 ± 1.17 in 2010 to 1.37 ± 1.21 in 2014. In particular, we observed an increase in the prevalence of cardiovascular failure (from 27.23% in 2010 to 28.92% in 2014), respiratory failure (from 32.24% in 2010 to 37.49% in 2014), renal failure (from 24.18% in 2010 to 30.33% in 2014), and hepatic failure (from 3.16% in 2010 to 4.11% in

Table 1

Sociodemographic and clinical characteristics of patients hospitalized who suffered a ventilator-associated pneumonia (VAP) in Spain from 2010 to 2014.

		2010	2011	2012	2013	2014	Total	*P*
Number of hospital admissions with VAP		1774	2065	1852	1871	1774	9336	.041
Incidence of VAP per 100,000 inhabitants*		41.7	47.45	42.82	43.46	40.55	43.2	
Patients that required invasive mechanical ventilation		45,132	46,499	45,342	45,534	44,686	227,193	.387
Incidence of VAP per mechanically ventilated patients (%)		3.93	4.44	4.08	4.11	3.97	4.11	
Sex	Female, n (%)	544 (30.67)	611 (29.59)	540 (29.16)	564 (30.14)	550 (31)	2809 (30.09)	.736
Age, mean (SD)		58.45 (17.97)	58.52 (18.37)	58.23 (18.45)	58.28 (18.34)	58.01 (18.44)	58.3 (18.31)	.925
Age groups, y	<25, n (%)	91 (5.13)	121 (5.86)	110 (5.94)	112 (5.99)	107 (6.03)	541 (5.79)	.336
	25–34, n (%)	112 (6.31)	118 (5.71)	97 (5.24)	79 (4.22)	83 (4.68)	489 (5.24)	
	35–44, n (%)	155 (8.74)	187 (9.06)	154 (8.32)	148 (7.91)	160 (9.02)	804 (8.61)	
	45–54, n (%)	272 (15.33)	307 (14.87)	290 (15.66)	327 (17.48)	292 (16.46)	1488 (15.94)	
	55–64, n (%)	358 (20.18)	395 (19.13)	392 (21.17)	386 (20.63)	360 (20.29)	1891 (20.25)	
	65–74, n (%)	428 (24.13)	509 (24.65)	441 (23.81)	467 (24.96)	433 (24.41)	2278 (24.4)	
	75–84, n (%)	330 (18.6)	397 (19.23)	331 (17.87)	318 (17)	321 (18.09)	1697 (18.18)	
	≥85, n (%)	28 (1.58)	31 (1.5)	37 (2)	34 (1.82)	18 (1.01)	148 (1.59)	
Acute myocardial infarction, n (%)		135 (7.61)	132 (6.39)	150 (8.1)	143 (7.64)	104 (5.86)	664 (7.11)	.040
Congestive heart failure, n (%)		224 (12.63)	235 (11.38)	265 (14.31)	293 (15.66)	263 (14.83)	1280 (13.71)	.001
Peripheral vascular disease, n (%)		109 (6.14)	112 (5.42)	104 (5.62)	103 (5.51)	111 (6.26)	539 (5.77)	.734
Cerebrovascular disease, n (%)		354 (19.95)	456 (22.08)	368 (19.87)	394 (21.06)	397 (22.38)	1969 (21.09)	.197
Hemiplegia or paraplegia, n (%)		165 (9.3)	196 (9.49)	170 (9.18)	183 (9.78)	177 (9.98)	891 (9.54)	.922
Dementia, n (%)		4 (0.23)	12 (0.58)	7 (0.38)	8 (0.43)	5 (0.28)	36 (0.39)	.430
Chronic obstructive pulmonary disease, n (%)		205 (11.56)	235 (11.38)	226 (12.2)	228 (12.19)	239 (13.47)	1133 (12.14)	.325
Rheumatoid disease, n (%)		15 (0.85)	18 (0.87)	15 (0.81)	12 (0.64)	18 (1.01)	78 (0.84)	.811
Peptic ulcer, n (%)		39 (2.2)	34 (1.65)	34 (1.84)	40 (2.14)	26 (1.47)	173 (1.85)	.413
Mild liver disease, n (%)		124 (6.99)	137 (6.63)	138 (7.45)	124 (6.63)	133 (7.5)	656 (7.03)	.725
Moderate/severe liver disease, n (%)		23 (1.3)	43 (2.08)	45 (2.43)	39 (2.08)	25 (1.41)	175 (1.87)	.053
Renal disease, n (%)		77 (4.34)	100 (4.84)	89 (4.81)	104 (5.56)	84 (4.74)	454 (4.86)	.544
Diabetes, n (%)		204 (11.5)	226 (10.94)	204 (11.02)	191 (10.21)	164 (9.24)	989 (10.59)	.210
Diabetes with complications, n (%)		22 (1.24)	27 (1.31)	30 (1.62)	35 (1.87)	25 (1.41)	139 (1.49)	.499
Cancer, n (%)		104 (5.86)	156 (7.55)	131 (7.07)	117 (6.25)	103 (5.81)	611 (6.54)	.113
Metastatic cancer, n (%)		45 (2.54)	59 (2.86)	47 (2.54)	45 (2.41)	34 (1.92)	230 (2.46)	.456
Acquired immunodeficiency syndrome, n (%)		12 (0.68)	22 (1.07)	17 (0.92)	16 (0.86)	8 (0.45)	75 (0.8)	.261
CCI index, mean (SD)		1.05 (0.98)	1.07 (0.98)	1.1 (0.99)	1.11 (0.98)	1.08 (1)	1.08 (0.98)	.318
PD: Cranial hemorrhage, n (%)		261 (14.71)	342 (16.56)	255 (13.77)	274 (14.64)	286 (16.12)	1418 (15.19)	.097
PD: Heart disease, n (%)		224 (12.63)	219 (10.61)	233 (12.58)	219 (11.7)	180 (10.15)	1075 (11.51)	.056
PD: Vein or artery occlusion, n (%)		99 (5.58)	128 (6.2)	108 (5.83)	147 (7.86)	139 (7.84)	621 (6.65)	.006
PD: Cranial or spine fracture, n (%)		137 (7.72)	158 (7.65)	139 (7.51)	129 (6.89)	107 (6.03)	670 (7.18)	.239
PD: Pulmonary disease or pneumonia, n (%)		101 (5.69)	120 (5.81)	101 (5.45)	80 (4.28)	84 (4.74)	486 (5.21)	.153
PD: Cancer, n (%)		97 (5.47)	132 (6.39)	121 (6.53)	109 (5.83)	83 (4.68)	542 (5.81)	.108

P value for time trend using Poisson or logistic regression adjusted by age and sex when appropriate.
CCI = Charlson comorbidity index, PD = primary diagnosis.
* Incidence calculated over total number of hospitalizations in Spain that year.

2014). However, neurological and hematological failures did not change significantly over time (Table 2).

Within the pathogens analyzed, the most commonly found was *Pseudomonas* (5.68%), followed by other Gram-negative bacteria (4.93%), *Klebsiella pneumonia* (2.89%), *Staphylococcus aureus* susceptible to methicillin (2.86%), candidiasis (2.57%), *Streptococcus pneumoniae* (2.32%), *Escherichia coli* (1.83%), *Haemophilus influenzae* (1.74%), and *S. aureus* resistant to methicillin (1.16%). We did not find significant differences in the isolation of these microorganisms over time. All other pathogens were found in less than 1% of patients (Table 2).

Over the entire time period, IHM was 34.88%. It significantly decreased during the study period, from 35.74% in 2010 to 32.81% in 2014. Table 3 summarizes sociodemographic and clinical characteristics of patients who suffered a VAP according to hospitalization survival. Mortality was higher in males, in older patients, and in those with congestive heart failure, COPD, rheumatoid disease, peptic ulcer, hepatic or renal disease, diabetes with complications, cancer (including metastatic cancer), and AIDS. IHM was also higher when the primary diagnosis was one of the following: vein or artery occlusion, pulmonary disease, and cancer. By contrast, hospital mortality was lower when the primary diagnosis was cranial hemorrhage and cranial or spine fracture.

Table 4 summarizes procedures, hospital outcomes, acute organ failures, and pathogen isolations in patients hospitalized with VAP according to hospitalization survival. IHM was higher in patients who underwent bronchoscopy, in subjects receiving transfusion, in individuals treated with dialysis, or in those who were readmitted. Patients with acute organ failures (including cardiovascular, respiratory, neurological, hematologic, hepatic, and renal organ failures) also had a higher mortality than those without organ failure. Regarding pathogens isolated, only documented Aspergillosis was associated with increased IHM. As expected, when we grouped all species associated with rising IHM, this variable was associated with higher IHM 39.12% for those with any of these pathogens versus 33.97% for those without.

Table 2

Procedures, hospital outcomes, organ failures, and pathogen isolations of patients hospitalized who suffered a ventilator-associated pneumonia in Spain from 2010 to 2014.

	2010	2011	2012	2013	2014	Total	*P*
Thoracentesis, n (%)	59 (3.33)	65 (3.15)	57 (3.08)	61 (3.26)	58 (3.27)	300 (3.21)	.993
Pleural drainage tube, n (%)	216 (12.18)	238 (11.53)	191 (10.31)	199 (10.64)	182 (10.26)	1026 (10.99)	.264
Bronchoscopy, n (%)	226 (12.74)	291 (14.09)	286 (15.44)	309 (16.52)	296 (16.69)	1408 (15.08)	.003
Transfusion, n (%)	482 (27.17)	543 (26.3)	525 (28.35)	536 (28.65)	508 (28.64)	2594 (27.78)	.374
Dialysis, n (%)	187 (10.54)	237 (11.48)	205 (11.07)	211 (11.28)	239 (13.47)	1079 (11.56)	.068
Tracheostomy, n (%)	843 (47.52)	998 (48.33)	867 (46.81)	846 (45.22)	789 (44.48)	4343 (46.52)	.101
Pressure ulcers, n (%)	117 (6.6)	138 (6.68)	145 (7.83)	111 (5.93)	109 (6.14)	620 (6.64)	.168
Undergone surgery, n (%)	1369 (77.17)	1595 (77.24)	1405 (75.86)	1399 (74.77)	1306 (73.62)	7074 (75.77)	.044
Emergency room admission, n (%)	1446 (81.51)	1682 (81.45)	1530 (82.61)	1508 (80.6)	1456 (82.07)	7622 (81.64)	.589
Readmission, n (%)	125 (7.05)	150 (7.26)	158 (8.53)	153 (8.18)	150 (8.46)	736 (7.88)	.298
In-hospital mortality, n (%)	634 (35.74)	756 (36.61)	658 (35.53)	626 (33.46)	582 (32.81)	3256 (34.88)	.070
Septic shock, n (%)	352 (19.84)	395 (19.13)	353 (19.06)	386 (20.63)	335 (18.88)	1821 (19.51)	.646
Vascular organ failure, n (%) (%)	483 (27.23)	571 (27.65)	560 (30.24)	586 (31.32)	513 (28.92)	2713 (29.06)	.029
Respiratory organ failure, n (%)	572 (32.24)	687 (33.27)	622 (33.59)	705 (37.68)	665 (37.49)	3251 (34.82)	.000
Neurological organ failure N (%)	176 (9.92)	216 (10.46)	208 (11.23)	201 (10.74)	172 (9.7)	973 (10.42)	.560
Hematologic organ failure, n (%)	134 (7.55)	170 (8.23)	135 (7.29)	136 (7.27)	131 (7.38)	706 (7.56)	.766
Hepatic organ failure, n (%) (%)	56 (3.16)	67 (3.24)	95 (5.13)	73 (3.9)	73 (4.11)	364 (3.9)	.013
Renal organ failure, n (%)	429 (24.18)	553 (26.78)	525 (28.35)	550 (29.4)	538 (30.33)	2595 (27.8)	.000
Number of organ failures, mean (SD)	1.24 (1.17)	1.29 (1.1)	1.35 (1.20)	1.41 (1.29)	1.37 (1.21)	1.33 (1.18)	.002
Pseudomonas, n (%)	102 (5.75)	112 (5.42)	106 (5.72)	119 (6.36)	91 (5.13)	530 (5.68)	.575
Other Gram negatives bacteria, n (%)	100 (5.64)	96 (4.65)	109 (5.89)	81 (4.33)	74 (4.17)	460 (4.93)	.050
Klebsiella pneumoniae, n (%)	61 (3.44)	58 (2.81)	51 (2.75)	49 (2.62)	51 (2.87)	270 (2.89)	.633
Staphylococcus aureus sensible to methicillin, n (%)	55 (3.1)	69 (3.34)	44 (2.38)	59 (3.15)	40 (2.25)	267 (2.86)	.160
Staphylococcus aureus resistant to methicillin, n (%)	28 (1.58)	20 (0.97)	28 (1.51)	18 (0.96)	14 (0.79)	108 (1.16)	.086
Candidiasis, n (%)	54 (3.04)	51 (2.47)	43 (2.32)	44 (2.35)	48 (2.71)	240 (2.57)	.624
Streptococcus pneumoniae, n (%)	56 (3.16)	50 (2.42)	35 (1.89)	38 (2.03)	38 (2.14)	217 (2.32)	.091
Escherichia coli, n (%)	36 (2.03)	34 (1.65)	40 (2.16)	26 (1.39)	35 (1.97)	171 (1.83)	.390
Haemophilus influenzae, n (%)	33 (1.86)	36 (1.74)	33 (1.78)	28 (1.5)	32 (1.8)	162 (1.74)	.930
Aspergilosis, n (%)	8 (0.45)	25 (1.21)	20 (1.08)	19 (1.02)	19 (1.07)	91 (0.97)	.156
Nonspecified *Streptococcus*, n (%)	14 (0.79)	8 (0.39)	17 (0.92)	16 (0.86)	11 (0.62)	66 (0.71)	.275

P value for time trend using logistic regression adjusted by age and sex.

We can see the results of the multivariate analysis of factors independently associated with IHM among hospitalized patients who suffered VAP in Spain from 2010 to 2014 in Table 5. IHM was significantly higher in males, in older subjects, in patients with comorbidities, in those undergoing surgery, and in patients with one of the following primary diagnosis: vein or artery occlusion, pulmonary disease or pneumonia, and cancer. Mortality was also significantly higher in patients with emergency room admissions and those who were readmitted. By contrast, IHM was significantly lower in patients in which primary diagnosis was cranial hemorrhage and cranial or spine fracture.

Time-trend analysis showed a significant decrease in IHM in patients admitted with VAP in Spain from 2010 to 2014.

4. Discussion

Our results show that the rate of hospitalization for VAP has decreased significantly from 2010 to 2014 in Spain. Other authors have reported similar trends.[12,21] These results might reflect efficiency of preventive measures and critical care practices. In fact, VAP prevention bundle is one of the major strategies used for reducing the incidence of this condition.[14,22] It includes the following components: medical education, use of subglottic suction endotracheal tubes, semi-recumbent position, sedation protocols for rapid weaning, and oral care with chlorhexidine.[23,24] Despite all, it has been demonstrated that there is a wide variability in compliance with VAP-preventive measures across intensive care units in Europe.[25] Apart from compliance with VAP prevention bundles, the rising part of noninvasive ventilation support (noninvasive mechanical ventilation and high flow oxygen therapy) might also explain the decreasing incidence of VAP.

In agreement with other reports, our study showed a male predominance.[26–28] Male sex is one of the nonmodifiable patient-related risk factors for the development of VAP along with others such as preexisting pulmonary disease, AIDS, coma, head trauma, and multiple-organ system failure.[29]

The rising use of bronchoscopies in our study is remarkable, whereas the best ways to get microbiological diagnosis in VAP are still discussed. Moreover, it is not clear the why the use of bronchoscopy is associated with mortality. It is possible that this procedure is performed more frequently in patients with a worse clinical course, in order to optimize antibiotic treatment.

We also found an increase in the number of organ failures over time. Specifically, we showed an increased failure of vascular, respiratory, hepatic, and renal organs during the study period. It has been found that multiple organ dysfunction, along with a possible immunosuppression and other underlying diseases, increases the risk of opportunistic infections.[30]

According to our results, Gram-negative bacteria were the most frequently isolated pathogens with *Pseudomonas* showing the highest prevalence (5.68%). Furthermore, its dominance did not change over time. Other authors have also found that *Pseudomonas aeruginosa* (PA) is one of the most common bacteria causing VAP,[31,32] with a prevalence of approximately

Table 3

Sociodemographic and clinical characteristics of patient hospitalized who suffered a ventilator-associated pneumonia according to hospitalization survival in Spain, 2010–2014.

		Live, n	Died, n	IHM* 100	*P*
Total		6080	3256	34.88	NA
Sex	Male	4217	2310	35.39	.002
	Female	1863	946	33.68	
Age groups, y	<25	474	67	12.38	<.001
	25–34	417	72	14.72	
	35–44	647	157	19.53	
	45–54	1111	377	25.34	
	55–64	1232	659	34.85	
	65–74	1322	956	41.97	
	75–84	799	898	52.92	
	85+	78	70	47.3	
Acute myocardial infarction	No	5673	2999	34.58	.755
	Yes	407	257	38.7	
Congestive heart failure	No	5355	2701	33.53	.011
	Yes	725	555	43.36	
Peripheral vascular disease	No	5756	3041	34.57	.801
	Yes	324	215	39.89	
Cerebrovascular disease	No	4755	2612	35.46	.025
	Yes	1325	644	32.71	
Hemiplegia or paraplegia	No	5357	3088	36.57	<.001
	Yes	723	168	18.86	
Dementia	No	6068	3232	34.75	.051
	Yes	12	24	66.67	
Chronic obstructive pulmonary disease	No	5418	2785	33.95	.048
	Yes	662	471	41.57	
Rheumatoid disease	No	6040	3218	34.76	.042
	Yes	40	38	48.72	
Peptic ulcer	No	5986	3177	34.67	.045
	Yes	94	79	45.66	
Mild liver disease	No	5745	2935	33.81	<.001
	Yes	335	321	48.93	
Moderate/severe liver disease	No	6017	3144	34.32	<.001
	Yes	63	112	64	
Renal disease	No	5869	3013	33.92	<.001
	Yes	211	243	53.52	
Diabetes	No	5483	2864	34.31	.317
	Yes	597	392	39.64	
Diabetes with complications	No	6011	3186	34.64	.016
	Yes	69	70	50.36	
Cancer	No	5777	2948	33.79	<.001
	Yes	303	308	50.41	
Metastatic cancer	No	5968	3138	34.46	<.001
	Yes	112	118	51.3	
Acquired immunodeficiency syndrome, n (%)	No	6038	3223	34.8	<.001
	Yes	42	33	44	
PD: Cranial hemorrhage	No	5076	2842	35.89	<.001
	Yes	1004	414	29.2	
PD: Heart disease	No	5417	2844	34.43	.285
	Yes	663	412	38.33	
PD: Vein or artery occlusion	No	5743	2972	34.1	<.001
	Yes	337	284	45.73	
PD: Cranial or spine fracture	No	5527	3139	36.22	<.001
	Yes	553	117	17.46	
PD: Pulmonary disease or pneumonia	No	5841	3009	34	<.001
	Yes	239	247	50.82	
PD: Cancer	No	5791	3003	34.15	<.001
	Yes	289	253	46.68	

P value to assess differences in IHM using logistic regression adjusted by age and sex when appropriate.
IHM = in-hospital mortality, PD = primary diagnosis.

Table 4

Procedures, hospital outcomes, organ failures, and pathogen isolations in patient hospitalized who suffered a ventilator-associated pneumonia according to hospitalization survival in Spain, 2010–2014.

		Live	Died	IHM*100	*P*
Thoracentesis	No	5898	3138	34.73	.176
	Yes	182	118	39.33	
Pleural drainage tube	No	5409	2901	34.91	.243
	Yes	671	355	34.6	
Bronchoscopy	No	5191	2737	34.52	.019
	Yes	889	519	36.86	
Transfusion	No	4565	2177	32.29	<.001
	Yes	1515	1079	41.6	
Dialysis	No	5646	2611	31.62	<.001
	Yes	434	645	59.78	
Tracheostomy	No	3236	1757	35.19	.025
	Yes	2844	1499	34.52	
Pressure ulcers	No	5638	3078	35.31	<.001
	Yes	442	178	28.71	
Undergone surgery	No	1419	843	37.27	<.001
	Yes	4661	2413	34.11	
Emergency room admission	No	1099	615	35.88	.560
	Yes	4981	2641	34.65	
Readmission	No	5684	2916	33.91	<.001
	Yes	396	340	46.2	
Septic shock	No	5324	2191	29.16	<.001
	Yes	756	1065	58.48	
Vascular organ failure	No	4815	1808	27.3	<.001
	Yes	1265	1448	53.37	
Respiratory organ failure	No	4305	1780	29.25	<.001
	Yes	1775	1476	45.4	
Neurological organ failure	No	5489	2874	34.37	.001
	Yes	591	382	39.26	
Hematologic organ failure	No	5763	2867	33.22	<.001
	Yes	317	389	55.1	
Hepatic organ failure	No	5947	3025	33.72	<.001
	Yes	133	231	63.46	
Renal organ failure	No	4915	1826	27.09	<.001
	Yes	1165	1430	55.11	
Pseudomonas	No	5757	3049	34.62	.159
	Yes	323	207	39.06	
Other gram-negatives bacteria	No	5797	3079	34.69	.160
	Yes	283	177	38.48	
Klebsiella pneumoniae	No	5911	3155	34.8	.270
	Yes	169	101	37.41	
Staphylococcus aureus sensible to methicillin	No	5895	3174	35	.827
	Yes	185	82	30.71	
Staphylococcus aureus resistant to methicillin	No	6013	3215	34.84	.905
	Yes	67	41	37.96	
Candidiasis	No	5934	3162	34.76	.371
	Yes	146	94	39.17	
Streptococcus pneumoniae	No	5935	3184	34.92	.678
	Yes	145	72	33.18	
Escherichia coli	No	5971	3194	34.85	.960
	Yes	109	62	36.26	
Haemophilus influenzae	No	5960	3214	35.03	.029
	Yes	120	42	25.93	
Aspergilosis	No	6042	3203	34.65	<.001
	Yes	38	53	58.24	
Non specified *Streptococcus*	No	6030	3240	34.95	.151
	Yes	50	16	24.24	
All species that increased IHM*	No	5096	2622	33.97	.004
	Yes	984	634	39.12	

P value to assess differences in IHM using logistic regression adjusted by age and sex.

IHM = in-hospital mortality.

* All pathogens exception made of *Staphylococcus aureus* sensible to methicillin, *Streptococcus pneumoniae*, *Haemophilus influenzae*, and nonspecified Streptococcus.

Table 5

Factors independently associated with in-hospital mortality among patient hospitalized who suffered a ventilator-associated pneumonia in Spain, 2010–2014.

		Odds ratio (OR)	95% CI
Sex	Female	1	
	Male	1.16	(1.05–1.28)
Age group, y	<25	1	
	25–34	1.15	(0.80–1.65)
	35–44	1.51	(1.10–2.07)
	45–54	2.02	(1.51–2.70)
	55–64	3.11	(2.35–4.13)
	65–74	4.12	(3.12–5.44)
	75–84	6.14	(4.64–8.14)
	≥85	3.82	(2.50–5.84)
Charlson comorbidity index		1.09	(1.04–1.15)
PD: Cranial hemorrhage		0.80	(0.69–0.91)
PD: Vein or artery occlusion		1.48	(1.24–1.77)
PD: Cranial or spine fracture		0.57	(0.46–0.71)
PD: Pulmonary disease or pneumonia		1.81	(1.49–2.21)
PD: Cancer		1.52	(1.24–1.86)
Undergone surgery		1.14	(1.02–1.28)
Emergency room admission		1.15	(1.03–1.31)
Readmission		1.45	(1.23–1.71)
Year		0.95	(0.92–0.98)

OR obtained using logistic regression adjusted by all study variables significant in the bivariable analysis. Only those with significant ORs are shown.
95% CI = 95% confidence interval, PD = primary diagnosis.

4%.[33] In addition, VAP caused by PA has been associated with higher case fatality rates than that by other bacteria.[34]

The relatively low part of methicillin-resistant *Staphylococcus aureus* has to be pointed out as an element of European epidemiology during the last years that may be different elsewhere.

The low percentage of cases is surprising in which there is an isolated microorganism. It may be because the techniques used to obtain microbiologic specimens, such as bronchoscopy examinations, are not routinely performed in clinical practice, as it has been found in other studies.[13]

IHM decreased over time among patients with a diagnosis of VAP in our study, despite the significant increase in mean number of acute organ failures during this period, which could be due to an improvement in the management of these patients over time. These data corroborate to previous studies. In a population-based cohort, the hospital mortality decreased significantly during a 7-year study period.[13] Rosenberger et al [35] also showed that mortality following an episode of VAP decreased over time and attributed this to advancements in pulmonary and general critical care rather than any specific interventions.

We found a higher mortality in males, in the elderly subgroups, in patients undergoing surgery, and in those with underlying diseases. In fact, CCI was independently associated with an increased risk of IHM in our study. Tseng et al [36] also showed that high CCI, as well as high Sequential Organ Failure Assessment (SOFA) score, significantly affect hospital mortality in patients with VAP. The isolation of Aspergillus was also associated with increased IHM.

In our study of VAP patients, IHM was higher when principal diagnosis was occlusion of a vessel, pulmonary disease, or cancer. Malignancy has also been reported as a prognostic indicator of hospital mortality in a recent study.[37] Patients with cancer are at a high risk of infections and subsequent complications. Identified risk factors for VAP in cancer patients include age (≥65 years), surgery, and tracheostomy.[38] On the contrary, IHM was lower when principal diagnosis was cranial hemorrhage or cranial or spinal fracture. Cinotti et al [39] found that among patients suffering from subarachnoid hemorrhage, longer ICU stay and time with mechanical ventilation increased the risk of VAP, but not of mortality.

Other factor independently associated with IHM mortality among patients hospitalized with VAP in the present study was emergency room admission. Prior reports that have examined the effect of boarding on intensive care unit outcomes, including VAP, have found an association between increased emergency department LOHS with poor outcome.[40,41] Thus, for example, it has been demonstrated that in blunt trauma patients who are emergently intubated, increased emergency department length of stay is an independent risk factor for pneumonia. VAP interventions, successful in the intensive care unit, should be implemented early in the hospital course, and efforts should be made to minimize hospital crowding and emergency department length of stay.[40]

Readmission increases the risk of IHM after VAP in our population. In a retrospective case–control study, patients in the VAP group had a greater number of readmissions than the control group patients.[42]

This study examines the impact of VAP across the Spanish health care system rather than at an institutional level. The strengths of our findings lie in the large sample size, the 5-year follow-up period, and the standardized methodology, which has been used to investigate VAP and its complications.[7,42] Nevertheless, our study has some limitations. Our data source was the SNHDD, an administrative database that uses information the physician has included in the discharge report. Administrative data can be inaccurate for detection of hospital-acquired infections, including VAP. A systematic review by Goto et al [16] included 2 studies for VAP and both reported low to moderate sensitivity (42–72%) and moderate to high specificity (82–92%). It is unclear how this may affect the results of the study. Regardless, as the methodology has remained

constant throughout the study, we consider that changes detected over time are valuable. Furthermore, as the database does not include dates for diagnosis or procedures, it fails to establish a temporal relationship between the procedures, surgeries, septic shock, and pressure ulcers in the patients with VAP. Also, it is not possible to determine whether comorbidities were already present when the patient was admitted or may have appeared during the hospital stay. However, it is logical to think that chronic conditions (i.e., diabetes, COPD, etc) were present by the time of admission. Finally, our findings are limited by the lack of data, including, among others, severity of illness, antimicrobial therapy, specimen quality, and length of stay in the intensive care unit. These and other factors that may influence in VAP outcomes could not be analyzed.

In addition, we cannot identify whether changes in the use of strategies to prevent VAP during the study period may have had an influence on the results.

The study is limited by the fact that if a patient was admitted in the same year twice or more times, this event could not be detected; this is a consequence of the anonymity of the database. Furthermore, if a patient is transferred from one to another hospital, it would also be counted as 2 different admissions. However, the SNHDD has proved to be useful for epidemiological investigation, covers over 98% of hospital admission in Spain, and the Ministry of Health conducts periodical audits to warrantee its validity.[17,43] The code for VAP was first used in the SNHDD in 2010, so some underreporting in the first years could be expected.

In conclusion, this study shows that the incidence of VAP among hospitalized patients has decreased in Spain from 2010 to 2014.The IHM has also decreased over the study period. These results indicate that both prevention and management of VAP have probably got better in Spain during the study period.

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References

[1] Shitrit P, Meirson M, Mendelson G, et al. Intervention to reduce ventilator-associated pneumonia in individuals on long-term ventilation by introducing a customized bundle. J Am Geriatr Soc 2015;63:2089–93.
[2] Kalil AC, Metersky ML, Klompas M, et al. Management of adults with hospital-acquired and ventilator-associated pneumonia: 2016 Clinical Practice Guidelines by the Infectious Diseases Society of America and the American Thoracic Society. Clin Infect Dis 2016;63:575–82.
[3] Dudeck MA, Horan TC, Peterson KD, et al. National Healthcare Safety Network report, data summary for 2011, device-associated module. Am J Infect Control 2013;41:286–300.
[4] Dudeck MA, Horan TC, Peterson KD, et al. National Healthcare Safety Network (NHSN) Report, data summary for 2010, device-associated module. Am J Infect Control 2011;39:798–816.
[5] Wang Y, Eldridge N, Metersky ML, et al. National trends in patient safety for four common conditions, 2005-2011. N Engl J Med 2014;370:341–51.
[6] Muscedere JG, Day A, Heyland DK, et al. Attributable mortality, and clinical events as end points for clinical trials of ventilator-associated pneumonia and hospital-acquired pneumonia. Clin Infect Dis 2010;51 (Suppl 1):S120–5.
[7] Kollef MH, Hamilton CW, Ernst FR. Economic impact of ventilator-associated pneumonia in a large matched cohort. Infect Control Hosp Epidemiol 2012;33:250–6.
[8] American Thoracic Society; Infectious Diseases Society of America. 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.
[9] Melsen WG, Rovers MM, Koeman M, et al. Estimating the attributable mortality of ventilator-associated pneumonia from randomized prevention studies. Crit Care Med 2011;39:2736–42.
[10] Melsen WG, Rovers MM, Groenwold RH, et al. Attributable mortality of ventilator-associated pneumonia: a meta-analysis of individual patient data from randomised prevention studies. Lancet Infect Dis 2013;13:665–71.
[11] Chittawatanarat K, Jaipakdee W, Chotirosniramit N, et al. Microbiology, resistance patterns, and risk factors of mortality in ventilator-associated bacterial pneumonia in a Northern Thai tertiary-care university based general surgical intensive care unit. Infect Drug Resist 2014;7:203–10.
[12] Zuschneid I, Schwab F, Geffers C, et al. Trends in ventilator-associated pneumonia rates within the German nosocomial infection surveillance system (KISS). Infect Control Hosp Epidemiol 2007;28:314–8.
[13] Ding S, Kilickaya O, Senkal S, et al. Temporal trends of ventilator-associated pneumonia incidence and the effect of implementing health-care bundles in a suburban community. Chest 2013;144:1461–8.
[14] Aggazzotti G, Ferrari E, Giovanardi C, et al. Trends in ventilator-associated pneumonia: impact of a ventilator care bundle in an Italian tertiary care hospital intensive care unit. Am J Infect Control 2014;42:1312–6.
[15] Choi JY, Kwak YG, Yoo H, et al. Trends in the incidence rate of device-associated infections in intensive care units after the establishment of the Korean Nosocomial Infections Surveillance System. J Hosp Infect 2015;91:28–34.
[16] Goto M, Ohl ME, Schweizer ML, et al. Accuracy of administrative code data for the surveillance of healthcare-associated infections: a systematic review and meta-analysis. Clin Infect Dis 2014;58:688–96.
[17] Instituto Nacional de Gestión Sanitaria, Ministerio de Sanidad, Servicios Sociales e Igualdad. Spanish National Hospital Discharge Database. Conjunto Mínimo Básico de Datos, Hospitales del INSALUD. Available at: http://www.ingesa.msc.es/estadEstudios/documPublica/CMBD-2001.htm. Accessed September 6, 2016.
[18] Charlson ME, Pompei P, Ales KL, et al. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. J Chronic Dis 1987;40:373–83.
[19] Jiménez-Trujillo I, Jiménez-García R, de Miguel-Díez J, et al. Incidence, characteristic and outcomes of ventilator-associated pneumonia among type 2 diabetes patients: an observational population-based study in Spain. Eur J Intern Med 2017;40:72–8.
[20] Instituto Nacional de Estadística. Population Estimates 2010. Available at: www.ine.es. Accessed September 6, 2016.
[21] El-Saed A, Al-Jardani A, Althaqafi A, et al. Ventilator-associated pneumonia rates in critical care units in 3 Arabian Gulf countries: a 6-year surveillance study. Am J Infect Control 2016;44:794–8.
[22] Al-Thaqafy MS, El-Saed A, Arabi YM, et al. Association of compliance of ventilator bundle with incidence of ventilator-associated pneumonia and ventilator utilization among critical patients over 4 years. Ann Thorac Med 2014;9:221–6.
[23] Pérez-Granda MJ, Muñoz P, Heras C, et al. Prevention of ventilator-associated pneumonia: can knowledge and clinical practice be simply assessed in a large institution? Respir Care 2013;58:1213–9.
[24] Ali HS, Khan FY, George S, et al. Epidemiology and outcome of ventilator-associated pneumonia in a heterogeneous ICU population in Qatar. Biomed Res Int 2016;2016:8231787.
[25] Kaier K, Lambert ML, Frank UK, et al. Impact of availability of guidelines and active surveillance in reducing the incidence of ventilator-associated pneumonia in Europe and worldwide. BMC Infect Dis 2014;14:199.
[26] Rello J, Ollendorf DA, Oster G, et al. Epidemiology and outcomes of ventilator-associated pneumonia in a large US database. Chest 2002;122:2115–21.
[27] Jaimes F, De La Rosa G, Gómez E, et al. Incidence and risk factors for ventilator-associated pneumonia in a developing country: where is the difference? Respir Med 2007;101:762–7.
[28] Resende MM, Monteiro SG, Callegari B, et al. Epidemiology and outcomes of ventilator-associated pneumonia in northern Brazil: an analytical descriptive prospective cohort study. BMC Infect Dis 2013;13:119.
[29] Bonten MJ, Kollef MH, Hall JB. Risk factors for ventilator-associated pneumonia: from epidemiology to patient management. Clin Infect Dis 2004;38:1141–9.
[30] Heredia-Rodríguez M, Peláez MT, Fierro I, et al. Impact of ventilator-associated pneumonia on mortality and epidemiological features of patients with secondary peritonitis. Ann Intensive Care 2016;6:34.
[31] Tumbarello M, De Pascale G, Trecarichi EM, et al. Clinical outcomes of Pseudomonas aeruginosa pneumonia in intensive care unit patients. Intensive Care Med 2013;39:682–92.

[32] Micek S, Johnson MT, Reichley R, et al. An institutional perspective on the impact of recent antibiotic exposure on length of stay and hospital costs for patients with gram-negative sepsis. BMC Infect Dis 2012;12: 56.
[33] Kollef MH, Chastre J, Fagon JY, et al. Global prospective epidemiologic and surveillance study of ventilator-associated pneumonia due to Pseudomonas aeruginosa. Crit Care Med 2014;42:2178–87.
[34] Tsay TB, Jiang YZ, Hsu CM, et al. Pseudomonas aeruginosa colonization enhances ventilator-associated pneumonia-induced lung injury. Respir Res 2016;17:101.
[35] Rosenberger LH, Hranjec T, McLeod MD, et al. Improvements in pulmonary and general critical care reduces mortality following ventilator-associated pneumonia. J Trauma Acute Care Surg 2013;74: 568–74.
[36] Tseng CC, Liu SF, Wang CC, et al. Impact of clinical severity index, infective pathogens, and initial empiric antibiotic use on hospital mortality in patients with ventilator-associated pneumonia. Am J Infect Control 2012;40:648–52.
[37] Inchai J, Pothirat C, Liwsrisakun C, et al. Ventilator-associated pneumonia: epidemiology and prognostic indicators of 30-day mortality. Jpn J Infect Dis 2015;68:181–6.
[38] Park SA, Cho SS, Kwak GJ. Factors influencing ventilator-associated pneumonia in cancer patients. Asian Pac J Cancer Prev 2014;15: 5787–91.
[39] Cinotti R, Dordonnat-Moynard A, Feuillet F, et al. Risk factors and pathogens involved in early ventilator-acquired pneumonia in patients with severe subarachnoid hemorrhage. Eur J Clin Microbiol Infect Dis 2014;33:823–30.
[40] Carr BG, Kaye AJ, Wiebe DJ, et al. Emergency department length of stay: a major risk factor for pneumonia in intubated blunt trauma patients. J Trauma 2007;63:9–12.
[41] Chalfin DB, Trzeciak S, Likourezos A, et al. Impact of delayed transfer of critically ill patients from the emergency department to the intensive care unit. Crit Care Med 2007;35:1477–83.
[42] Yang CC, Shih NC, Chang WC, et al. Long-term medical utilization following ventilator-associated pneumonia in acute stroke and traumatic brain injury patients: a case-control study. BMC Health Serv Res 2011;11:289.
[43] Ribera A, Marsal JR, Frreira-González I, et al. Predicting in-hospital mortality with coronary bypass surgery using hospital discharge data: comparison with a prospective observational study. Rev Esp Cardiol 2008;61:843–52.