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A Worldwide Perspective of Nursing Home-Acquired Pneumonia compared to Community-acquired Pneumonia

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Dr Liapikou, Dr Cilloniz and Dr Polverino contribute to the analysis of the cases and the writing of the article. We are all in the Dr Torres investigation group. Dr Peyrani P, Ramirez J, Menendez R, Torres A are all investigators of the CAPO study. Especially, Dr. Peyrani provides me all the data required from the CAPO database. Additionally, Dr Menendez and Dr Torres had reviewed the article.

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Abstract

BACKGROUND: Nursing home-acquired pneumonia (NHAP) is the leading cause of death among long-term care patients and the second most common cause of transfers to acute care facilities.

AIMS: The objective was to characterize the incidences, microbiology, and outcomes for hospitalized patients with community-acquired pneumonia (CAP) and NHAP.

METHODS: A secondary analysis of 5,160 patients from the Community-Acquired Pneumonia Organization (CAPO) database was performed. World regions were defined as North America (I), Latin America (II) and Europe (III).

RESULTS: From a total of 5,160 hospitalized patients with CAP, NHAP was identified in 287 (5.6%) patients. Mean age was 80 years old. NHAP distribution by region was 7% in region I, 3% in region II, 7% in region III. NHAP had more frequently neurological disease, D.M., congestive heart failure, renal failure than CAP patients (p<0,001). ICU admission was required in 32 (11%) patients. Etiology was defined in 68 (24%) patients with NHAP and 1,300 (27%) with CAP. The most common pathogens identified in NHAP included *Streptococcus pneumoniae* (31%), *Staphylococcus spp* (31%) and *Pseudomonas aeruginosa* (12%). The presentation of NHAP included more often pleural effusions (28% vs. 19%, p<0.001) and multilobar involvement (31% vs. 24%, p<0.001). The 30-day hospital mortality was statistically greater among patients with NHAP than among those with CAP (42% versus 18%; p < 0.001).

CONCLUSIONS: Worldwide, only a very small proportion of hospitalized CAP patients present with NHAP, whose poor outcomes may be primarily due to a higher number of comorbidities comparing to patients without NHAP.

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Keywords: pneumonia, respiratory infections, clinical epidemiology, quality of life, nursing homes.

Introduction

In many countries, the ageing of the population has led to increases in the number of disabled elderly persons, many of them residing in nursing homes (NH). It is estimated that over the next 30 years 40% of adults will spend some time in a long term care (LTC) facility before dying (1).

Nursing home–acquired pneumonia (NHAP) is the second most common infection among LTC patients and is responsible for the majority of transfers to emergency departments (2). More than 4 million NHAP cases are reported annually at a median incidence rate of 1–3.2 per 1000 patient-days, 600 000 emergency department admissions. Moreover, the mortality rates associated with NHAP are also higher than those associated with community-acquired pneumonia (CAP) and range from 5 to 40% (2).

There is little agreement, however, about the approach to managing NHAP. Patients with NHAP often suffer from more severe disease, with many comorbidities and functional status as the major determinant of survival (3). The appropriate management of NHAP remains questionable because of the controversial status of its microbial etiology. Data from the USA (4, 5, 6) indicate an excess of multidrug resistant (MDR) pathogens in patients with NHAP, but studies from Europe do not confirm this (7, 8, 9). Furthermore, the term NHAP has not the same meaning for all countries and this could explain discrepancies observed in

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patients' comorbidity patterns (especially aspiration), microbial etiology, diagnostic and treatment capabilities and management policies.

In an attempt to investigate some of the controversies in the field of NHAP, we performed a secondary analysis of the CAPO database (10) to evaluate the frequency of NHAP in hospitalized patients with CAP in different regions of the world and to compare severity, microbial patterns and outcomes between the two groups of hospitalized patients.

Methods

The CAPO Database

This database contains information regarding the management of 5,160 patients with CAP from 43 hospitals in 12 countries from June 2001 through September 2009. The study was approved but the Ethics Committee in each country and informed consent was waived because this was a retrospective, observational study. In each participating centre, primary investigators randomly selected 1 or more patients from a list of hospitalized patients with a diagnosis of CAP. Data were collected on a case report form and then entered into a computer and transferred electronically to the CAPO coordinating centre at the University of Louisville Clinical and Translational Research Support Centre. A sample of the data collection form is available at: www.caposite.com. Validation of data quality was performed at the study centre before each case was entered into the CAPO database.

The collected specimens included oropharyngeal swabs for polymerase chain

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reaction (PCR) and culture for virus and atypical pathogens, sputum and blood for culture, acute and convalescent serum samples for antibody titer determination for *Mycoplasma pneumoniae(* acute IgG titer >1:64), IgM titer (>1:16), *Chlamydia pneumoniae (*acute IgG titer (>1:512), IgM titer (>1:10)*and Legionella pneumophila(or* acute IgG, IgM, or IgA titer(>1:256), or a fourfold increase in either IgG or IgM in the convalescent specimen by immunofluorescent antibody assay. Urine specimens for *Legionella pneumophila* type 1antigen detection and *S pneumoniae* antigen as well. The samples are all collected according to the doctor's decisions and as part of each centre micro work up.

Definitions

A patient was considered to have *definitive CAP* if he meets the following criteria*:* a new pulmonary infiltrate on chest radiograph at time of hospitalization, plus at least one of the following: 1) a new or increased cough, 2) an abnormal temperature (<35.6ºC or >37.8ºC), or 3) an abnormal serum leukocyte count (leucocytosis, left shift, or leukopenia) as defined by local laboratory values.

The cause of CAP was declared if 1 of the following conditions was met: (1) positive findings for a bacterial pathogen in blood cultures; or (2) pathogen from endotracheal aspirate, bronchoscopy sample (protected brush or lavage), pleural fluid, or sputum cultures. Sputum cultures were restricted to sputum samples according to local hospital microbiology laboratory policy (eg, specimens must have < 25 squamous epithelial cells).

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Severity of disease was evaluated using the pneumonia severity index (PSI) and CURB-65 score. *Clinical stability* was defined per the American Thoracic Society guidelines for CAP (1) and the criteria for clinical stability were evaluated daily during the first 7 days of hospitalization. *In hospital all-cause mortality* was defined as the total mortality during hospitalization. *CAP-related mortality* was defined as death due primarily to the pulmonary infection during hospitalization.

Study regions were defined as USA/Canada (region I), Latin America (region II), Europe (region III) and Asia/Africa (region IV), as it has been done in a previous study of CAPO investigators (10).

NHAP is included under the concept of healthcare-associated pneumonia (HCAP) (6), referring only to patients presented with pneumonia at the emergencies residing in a nursing home or long-term care facility. These patients may have been received i.v. antibiotics the previous days from admission, but we don't have data for all the patients. The other risk factors for HCAP are not included in the NHAP group of patients (Hospitalization for 2 or more days in the preceding 90 days, family member with multidrug-resistant pathogen, chronic dialysis within 30 days and home wound care)

Statistical Analysis

Categorical variables were described with counts and percentages. For continuous variables, the mean ± SD was presented. Relationships between categorical variables were studied using the Chi-squared test or Fisher's exact test when necessary. The comparison of continuous variables between two groups was carried out using the t-test for unpaired data.

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Univariate and multivariate logistic regression analyses were performed to predict 30-day mortality (dependent variable). In the logistic regression models, we adjusted for region. The Hosmer-Lemeshow goodness-of-fit test was performed to assess the overall fit of the models.

All tests were two-tailed and significance was set at 5%. All analyses were performed with SPSS version 18.0 for Windows.

Results

During the study period, 5,160 adults with pneumonia were reviewed; 287 (5.6%) had NHAP. The proportions of NHAP among CAP patients for each region of the world are depicted in Table 1.

Demographics

The characteristics of patients with NHAP and CAP are compared in Table 2. Patients with NHAP were older (80.4±13.5 vs. 63.8±18.9 years, $p<0.001$), with 87.1% of NHAP patients >65 years, more women, less frequent smokers and had greater comorbidity than patients with CAP.

In the NHAP group, in region III higher proportion of patients had celebrovascular disorders (59% vs. 37% vs. 24.7%, for III,II, $p<0.001$, respectively) and in region II more patients had congestive heart failure (42% vs. 21.6% vs. 27%, for II($p<0.001$), I($p=0.723$), III($p=0.002$) respectively) and neurological disease (58% vs. 26% vs. 37%, for II, I, III, $p<0.001$,respectively). At the time of admission, more NHAP comparing to CAP patients had hospitalized for CAP the previous year (14.1% vs. 8.5%, $p=0.001$).

Etiology

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Etiology was defined in 68(24%) patients with NHAP and 1,333(27%) patients with CAP (Table 3). Blood cultures positive for pathogens considered causative of pneumonia were found in 1366 patients (35%) and sputum culture results were positive for 135 patients (4%) in the cohort. In NHAP patients, 68 blood cultures were positive for etiologic pathogen and 14 sputum cultures samples.

Overall, in NHAP patients, *S pneumoniae* and *Staphylococcus spp.* (MRSA and MSSA) were the most frequent causative pathogens. Predominantly*, Staphylococcus spp.* and especially *MRSA* is the most frequent pathogen in NHAP patients in region I (29.2% vs. 12.5% vs. 4.5%, p<0.001, p=0.005, p=0.613, respectively). Apart from *Legionella pneumophila* (two cases) in region III, atypical pathogens were rarely found in NHAP patients.

Pneumonia with polymicrobial etiology is more frequent in NHAP patients comparing to CAP, especially in region I (5. 2% vs. 3.1%, p=0. 014).

Severity assessment

NHAP was associated with more severe pneumonia, assessed according to the PSI (137±35.4 vs. 87.1±43.8, p<0.001). The proportion of patients classified as CURB-65 3-5 classes was around fourfold higher in the NHAP group (14.6% vs. 4%, p<0.001). The severity indices for regions I, II and III are presented in Table 4.

Mental confusion was detected more often in patients with NHAP (41.1% vs. 12.8%, p<0.001) such as multilobar infiltration (31% vs. 24.2%, p=0.010) and pleural effusion (28.2% vs. 19.3%, p<0.001).

The presentation of NHAP was more severe in Europe, prescribing with distribution of CURB65 3-5 classes (20.4% vs. 9.3% vs. 8.3%, p<0.001, p=0.02, p<0.001 respectively).

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Outcomes

Generally, clinical stability was reached after a mean of 4.8 ± 2.5 days of hospitalization. The mean time to clinical stability was 5.9 ± 2.5 days for NHAP comparing to 4.7 ± 2.5 days for those with CAP (p<0.001). The mean LOS of the cohort was 10±11 days (table 5).

Similar percentages of patients in the 2 groups required intensive care unit (ICU) admission (11.9% vs. 11.1%, p=0.704). From the view of regions, higher proportion of NHAP patients admitted to ICU in region II than the other parts of the world (28% vs. 14.4% vs. 4%, in II (p=0.09), I (p=0.92) and III (p=0.4), respectively), although the CAP related mortality was even higher in these patients (32.6% vs. 10.3% vs. 17%, II, I and III, p<0.001).

The overall hospital mortality rate was 9.3%, with NHAP mortality significally higher than CAP's mortality (26.1% vs. 8.3%, p<0.001). Even more, the one month mortality is even higher for NHAP patients (41.5% vs. 18.1%, p<0.001) compared to those with CAP.

Predictors of 30-day mortality

The multivariate analysis revealed that sex, neoplastic disease, cerebro-vascular disease, renal disease, neurological disease, aspiration, respiratory rate>30, multilobar pneumonia and NHAP were independently associated with increased 30-day mortality.

Discussion

The most important findings of this comparative report of NHAP were the following: 1) Patients with NHAP consist only a 5% of hospitalized CAP patients in the CAPO database, 2) Although, they presented with more severe pneumonia than CAP patients

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; received with the same frequency ICU care, 3) Comparing regions, the presentation of NHAP was more severe in Latin America and the proportion of patients admitted to ICU was also higher, but the mortality was highest also, 4) *S. pneumoniae* was the most frequent pathogen in both groups in the regions of the world except USA/Canada where *MRSA* was the prominent microorganism.

Presentation and severity

NHAP patients presented as expected with more comorbidities, especially with higher suspicity of aspiration as a consequence of neurological disorder(as dementia, Alzheimer disease, or psychotropic medications) and mental confusion as a crucial symptom.

The NHAP presentation was more severe than CAP's whether assessed by CURB-65 score, which has better performance accuracy in predicting mortality in NHAP patients (11). Especially in Europe, 20% of the NHAP cases belonged to CURB-65 3-5 classes (table 5). These differences reflect the differences in health care systems police and the assessment of severity of NHAP worldwide. A novel prognostic system, SOAR (systolic BP, oxygenation, age, and respiratory rate), is an alternative for better identification of severe NHAP (12, 13). One common limitation to all these scoring models is that none take into consideration the functional status of NH residents (3, 12).

Although, NHAP was more severe than CAP the proportion of patients admitted to the ICU was similar, except region II (28% vs. 18%, p=0.09). This study found that patients with NHAP were older, with higher frequency of comorbidities are more likely to have treatment restrictions, as do-not-resuscitate orders, meaning not to receive mechanical

ventilation or vasopressor support (14). Maybe in Latin America (region II) they have not these restrictions for social reasons. Another reason is the heterogeneity of the population residing in NH and the level of care in these institutions.

Etiology

The 2005 ATS/IDSA guidelines recommend that a patient with NHAP should receive empirical therapy including antibiotics directed against MDR microorganisms (*MRSA* and *Pseudomonas aeruginosa*) (6). The validity of these antimicrobial guidelines for the treatment of NH patients has been the most challenging because the microbiology of NHAP varies widely among published reports, according to study design, severity of illness and colonization with resistant organisms due to prior hospitalization.

Our results confirm the already published etiologic difference between NHAP from USA and Europe (7). Particularly, *Staphylococcus spp*. identified as the prominent pathogen in USA (52%), but *S pneumoniae* in Europe (46%) and Latin America (25%). Moreover, *S. aureus* and MRSA were significantly higher in the NHAP group than in the CAP group globally.

Studies from the USA indicate an excess of MDR pathogens in patients with NHAP (1, 2). In a study of El Solh et al, conducted in 52 NHAP patients who failed initial antimicrobial therapy, *S. aureus* (including *MRSA* strains) was found in 33%; enteric Gram(-) bacilli in 24%; and *P. aeruginosa* was found in 14% of isolates (16).

On the contrary, a recent Spanish study of Polverino et al (17), spanning 10 years of clinical experience confirmed the predominance of *S. pneumoniae* (58%) with *MRSA* representing only 5% of all isolates In agreement, an older study Lim et al (18) and the CAPNETZ study (19), reported that the most common pathogen in NHAP was also *S.*

pneumoniae (55%). In a similar design from Japan, Maruyama (20) and coworkers identified *C. pneumoniae*, *S. pneumoniae*, *Staphylococcus aureus*, and *influenza virus* as frequent causative agents of pneumonia in nonintubated institutionalized elderly. Interestingly, atypical pathogens accounted for 37% of all isolates.

The identification only of *Legionella pneumoniae* in region III in NHAP patients (9.1%), as the only atypical pathogen, is associated with the greater frequency of atypical pathogens in CAP also, in this region. However, it should be noted that outbreaks of *Legionella* infection have been reported in NH (3). Prospective clinical and environmental surveillance of NH has revealed previously unsuspected *Legionella* infection in association colonization of the facilities' water supply with *Legionella* (21).

Viral infection in NH is seasonal (22). In the present study, we also found seasonality of the epidemic of H1N1 in NHAP cases especially in region II (39% vs. 13%, p=0.16).

Outcomes

30-day mortality was far higher in NHAP patients comparing to CAP (41.5% vs. 18%, p<0.001), with 51% of NHAP died in region II, although 28% of them admitted to the ICU.

The higher mortality seen in NHAP patients may be due to the presence of dementia and other neurological disorders leading to atypical presentations of pneumonia and a delay in the diagnosis and treatment. In one study of patients with CAP aged 65> years the functional status for activities of daily living was being the best mortality predictor (23) and similar was concluded in others ones (17, 18, 20).

The other reason is the higher incidence of MDR bacteria and thus the administration of inappropriate empirical antibiotic treatment. In recent studies (24, 25, 26) enteral tube

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feeding (as well as poor functional status and aspiration) was predictive of MDR pathogens in NHAP. However, it is a fact that in clinical practice the poor functional status and the advanced age of these patients leads doctors to decide treatment restrictions, managing pneumonia as terminal event of a disabled adult.

Although the reasons are unknown, it is believed that differences in the populations of NHAP hospitalized patients between countries and regions result in differences in rates of mortality. In an attempt to indentify prognostic factors for mortality, in multiregresion analysis we found that comorbidities as cancer, neurological disease, renal disorder, celebrovascular disease and aspiration were significantly associated with death.

As an UK recent study of Chalmers et al (27) and the Spanish one of Rello and col (28) referring to pneumococcal severe HCAP, we did not found a relation of MDR pathogens and excess mortality.

One strength of our study is the generalizability of the CAPO database study population with an overall mortality rate of greater than 10%. The results of our multivariate analysis were consistent with the published literature indicating an increased risk for mortality in CAP patients with neurological disease, aspiration, multilobar infiltrates and NHAP (8).

The study has several limitations, including the retrospective design and the enrollment of nonconsecutive patients with CAP. Furthermore, the patients that were enrolled were limited to the specialized type of patients seen by each principal investigator. The study was limited to the five processes of care that were reviewed. Other processes of care, such as whether to perform a special procedure (e.g. bronchoscopy or parapneumonic effusion drainage) or when to admit to an intensive care unit, were not available in the

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database and may have been significant. Other important elements not available in our database were information about the functional status of the patients and data regarding treatment restrictions. Further, the proportion of patients with an etiology identified was low and did not exceed 30%, a proportion was expected because of the difficulty to obtain sputum specimens from elderly patients with confusion.

In conclusion, NHAP is a small proportion of CAP patients and in terms of etiology, severity and outcomes varies globally representing heterogeneity of administrative structures and treatment policies. As a consequence the management of these patients must take into account risk factors for mortality, functional status of the patient and microbiology of the community. This is one of the reasons for the low compliance of the doctors for the ATS/IDSA guidelines for HCAP (29) and the need for validation and reevaluation for the NHAP category.

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TABLES

Table 1. Incidence of NHAP

	Globally	*North America & Canada*	*Latin America*	*Europe*
		Region I	***Region II***	***Region III***
CAP	4873 (94.4%)	1534 (94.1%)	1383 (97.0%)	1900 (92.8%)
NHAP	287 (5.6%)	97 (5.9%)	43 (3.0%)	147 (7.2%)

Table 2. Characteristics of patients

Variables	**CAP n=4817, n (%)**	**NHAP n=287, n (%)**	*p-value*
Age (years), mean±SD	63.8±18.9	80.4±13.5	**<0.001**
Gender, male	2927 (60.8%)	137 (47.7%)	**<0.001**
Smoking status			**0.001**
Current	572 (26.5%)	14(15.7%)	
Ex-smokers	700 (32.4%)	20 (22.5%)	
No-smokers	887 (41.1%)	55 (61.8)	
Liver disease	279 (5.9%)	13 (4.6%)	0.366
Neurological Disease	509 (10.7%)	104 (36.4%)	**<0.001**
COPD	1230 (25.5%)	79 (27.5%)	0.453
Cancer	470 (9.9%)	31(10.9%)	0.573
HIV infection	214 (4.4%)	2 (0.7%)	**0.002**
DM	839 (17.6%)	64 (22.5%)	**0.035**
Congestic Heart Failure	848 (17.8%)	78 (27.5%)	**<0.001**
Renal disease	507 (10.7%)	53 (18.7%)	**<0.001**
Celebrovascular disease	618 (13%)	125 (44%)	**<0.001**

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Aspiration	253 (5.3%)	57 (20%)	**<0.001**
Prior admission for CAP	404 (8.5%)	40 (14.1%)	**0.001**
Time from symptoms until presentation, days	5.6±5.8	4±4.9	**0.009**
Prior antibiotics	783 (16.3%)	54 (18.9%)	0.244

Table 3. Etiological diagnosis

Subjects	**CAP** n =4817,(%)	**NHAP** n =287,(%)	**p-value**
Pathogen detected	1333(28%)	68(23%)	0,175
Mixed	124 (2,5%)	14 (5%)	0,024
Streptococcus pneumoniae	451 (37%)	17(32%)	0,386
Staphylococcus aureus	19 (1,6%)	3 (5,6%)	0,064
MRSA	38(3%)	9(17%)	<0,001
MSSA	40(3%)	6(11%)	0,012
GNB	150(12%)	11(20%)	0,095
Moraxella catarrhalis	28(2,3%)	3(5,6%)	0,143
Haemophilus influenzae	87(7%)	0	0,047
Mycoplasma pneumoniae.	30(2,5%)	0	0,636
Chlamydia pneumoniae	11(1%)	0	1
Legionella pneumophila	61(5%)	2(3,7%)	0,65
Klebsiella pneumoniae	38(3%)	0	0,404
Pseudomonas aeruginosa.	50(4%)	4(7,4%)	0,286
Escherichia coli	19(1,6%)	2(3,7%)	0,25

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Proteus spp	2(0,2%)	2(3,7%)	0,01
Influenza A virus	228	1	<0,001

MSSA: methicillin sensitive staphylococcus aureus. MRSA: methicillin resistant staph. Aureus, GNB: gram negative bacteria, NC: Not calculated

Table 4. Severity of CAP-NHAP by regions

Severity indices		**Globally**	**L. America**	**USA /Canada**	**Europe**
	CAP	n=4817	n =1383	n =1534	n =1900
	NHAP	n=287	n =43	n =97	n =147
PSI	CAP	87	80.3±45.1	84.2±43.0	94.5±42.5
			147.1 ± 37.1	128.5±32.0	139.7 ± 36.0
	NHAP	137	**<0.001**	**<0.001**	**<0.001**
	p-value	**<0,001**			
CURB-65	p-value	**<0,001**	**0.037**	**<0.001**	**<0.001**
0-1	CAP	4337	1235 (89.5%)	1474 (96.2%)	1572 (83.1%)
			38 (88.4%)	89 (91.8%)	164 (74.8%)
	NHAP	237	0.825	**0.031**	**0.011**
	p-value	**<0,01**			
2	CAP	330	104 (7.5%)	35(2.3%)	191 (10.1%)
			1 (2.3%)	0	7 (4.8%)
	NHAP	8	0.198	0.132	**0.035**
	p-value	**0,005**			
3-5	CAP	193	39 (3%)	23 (1.5%)	128 (6.7%)
	NHAP	42	4 (9.3%)	8 (8.3%)	20 (20.4%)
	p-value	**<0,001**	**0.022**	**<0.001**	**<0.001**
Confusion	CAP	616	193 (14%)	158 (10.3%)	265 (13.9%)
	NHAP	118	30 (69.8%)	37 (38.1%)	51 (34.7%)
	p-value	**<0,001**	**<0.001**	**<0.001**	**<0.001**
Time resp. symptoms	CAP	5,6 5,8	6.6±6.8	5.2±5.2	5±5. 2
	NHAP	4 4,9	4±2.4	3.8±5.5	4±5.1
	p-value	0,009	0.256	0.347	0.347
Multilobar infiltration	CAP	1178	95 (28.6%)	460 (30.1%)	310 (16.3%)
	NHAP	89	18 (41.9%)	36 (37.1%)	35 (23.8)
	p-value	**0,01**	0.060	0.146	**0.020**
Pleural Effusion	CAP	993	224 (16.2%)	297 (19.4%)	407 (21.5%)
	NHAP	81	6 (14%)	25 (25.8%)	50 (34%)
	p-value	**<0,001**	0.689	0.129	**<0.001**

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Table 5. Outcomes by regions

	Globally		**p-value**	**USA / Canada**		**p-value**	**Latin America**		**p-value**	**Europe**	
	CAP n=4817	**NHAP n=287**		**CAP NHAP n=1534**	**n=97**		**CAP n=1383**	**NHAP n=43**		**CAP n=1900**	**NHAP n=147**
In hospital mortality, n (%)	402 (8.3%)	75 (26.1%)	**<0.001**	88 (5.7%)	17 (17.5%)	**<0.001**	166 (12%)	19 (44.2%)	**<0.001**	148 (7.8%)	39 (39%)
30 day mortality, n (%)	871 (18.1%)	119 (41.5%)	**<0.001**	350 (22.8%) (45.4%)	44	**<0.001**	237 (17.1%)	22 (51.2%)	**<0.001**	284 (14.9%)	53 (36.1%)
CAP related death, n (%)	237 (4.9%)	49 (17.1%)	**<0.001**	45 (2.9%)	10 (10.3%)	**<0.001**	100 (7.2%)	14 (32.6%)	**<0.001**	92 (4.8%)	25 (17%)
LOS, mean±SD	10.1 ±11.1	10. 1 ±8.1	0.993	9.2 ±14.4	9.4 ±8.5	0.893	10.7 ±9.3	10 ±7.2	0.642	10.5 ±9	10.7 ±8.1
Admission ICU	573 (11.9%)	32 (11.9%)	0.704	216 (14.1%) (14.4%)	14	0.923	248 (17.9%)	12 (27.9%)	0.095	109 (5.7%)	6 (4.1%)
Stability day, mean±SD	4.7 ±2.5	5.9 ±2.5	**<0.001**	4.1 ±2.6	5.2 ±2.7	**<0.001**	5.2 ±2.5	6.3 ± 2.3	**0.004**	4.8 ±2.4	6.2 ±2.3
Readmission, n (%)	55 (1.1%)	5 (1.7%)	0.360	28 (1.8%)	2 (2.1%)	0.239	8 (0.6%)	0 0	0.617	19 (1%)	3 (1%)

LOS: length of hospital stay

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