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Gender differences in early versus late intensive care unit admission for community-acquired pneumonia patients

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UNIVERSITE JOSEPH FOURIER FACULTE DE MEDECINE DE GRENOBLE

Année : 2014 N°

**GENDER DIFFERENCIES IN EARLY VERSUS LATE
INTENSIVE CARE UNIT ADMISSION FOR COMMUNITY-
ACQUIRED PNEUMONIA PATIENTS**

Thèse présentée pour l'obtention du DOCTORAT EN MEDECINE

DIPLÔME D'ETAT

Par **Bastien BOUSSAT**

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Gender differences in early versus late intensive care unit admission for community-acquired pneumonia patients

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Résumé

Objectif: L'objectif de cette étude était d'étudier les différences de genre dans l'admission précoce et tardive des patients hospitalisés pour une pneumonie aiguë communautaire (PAC).

Méthodes: Nous avons réalisé une analyse *Post hoc* des données issues de deux études de cohorte prospectives multicentriques de patients adultes hospitalisés pour une PAC, EDCAP (Etats-Unis) et Pneumocom-1 (France). Le critère de jugement principal était le délai d'admission en réanimation ; précoce (admission le jour de la présentation aux urgences), tardive, pas d'admission. Le critère de jugement secondaire était la mortalité à 28 jours.

Résultats: Au total, 1368 hommes (53,8%) et 1190 femmes (46,2%) ont été inclus dans notre étude. Les patients hommes étaient plus sévères que les femmes (53,6% vs. 37,3% pour les classes IV et V du Pneumonia Severity Index). Les hommes avaient des taux plus élevés que les femmes pour l'admission en réanimation précoce (8,3% vs. 7,1%) et pour l'admission tardive (6,7% vs. 4,5%). Les hommes atteints de PAC sévère (classe V du Pneumonia Severity Index) bénéficiaient moins fréquemment d'une admission précoce en réanimation (17% vs. 26%) et étaient plus souvent admis tardivement (10% vs. 2%), comparativement aux femmes (p d'interaction = 0,02). La mortalité ne différait pas significativement entre les hommes et les femmes (7,5% vs. 6,5%), même après ajustement sur la sévérité et le délai d'admission en réanimation.

Conclusions: Cette étude démontre que les hommes atteints de PAC sévère sont admis plus tardivement en réanimation que les femmes et suggère l'existence d'un biais sexiste en faveur des femmes dans la prise en charge des patients atteints de PAC.

Mots-clés: pneumonie communautaire aiguë, genre, réanimation

Abstract

Objectives: The objective was to compare the early and late admission to intensive care unit (ICU) for male and female patients hospitalized with community-acquired pneumonia (CAP).

Methods: We performed a *Post hoc* analysis of the original data from the Emergency Department Community-Acquired Pneumonia and Pneumocom-1 prospective multicenter cohort studies of adult patients hospitalized with CAP. The primary endpoint was the ICU admission and timing: early (i.e., ICU admission on the day of emergency department presentation), late, and no ICU admission. The secondary endpoint was the 28-day mortality.

Results: 1,368 (53.5%) male patients and 1,190 (46.5%) female patients were included in sample analytical. Male patients were more severe than female patients (assigned to Pneumonia Severity Index classes IV-V; 53.6% vs. 37.3%) and had higher rates of early ICU admission (8.3% vs. 7.1%) and late ICU admission (6.7% vs. 4.5%). Men with severe CAP (Pneumonia Severity Index class V) had a lower rate of early ICU admission (17% vs. 26%), which was compensated by a higher percentage of late ICU admission (10% vs. 2%), compared to women (p for interaction = 0.02). Comparable 28-day mortality rates were observed for male and female patients, even after adjustment for severity and ICU admission timing.

Conclusions: This study suggests that male patients with severe CAP who require early ICU admission are less correctly identified than female patients. For the first time, a gender bias is highlighted in the process of care of CAP patients in favor of women.

Keywords: pneumonia, gender, intensive care, community-acquired infections

Introduction

Community-acquired pneumonia (CAP) is the sixth leading cause of death worldwide [1]. Considerable efforts have been made to reduce unnecessary care of less sick CAP patients [2-6]. Over the past decade, more attention has been paid to patients with severe CAP, such as those requiring care in an intensive care unit (ICU). Between 4 and 19 % of hospitalized patients with CAP are admitted to the ICU and the overall case-fatality rate for CAP inpatients is about 5% [6-8].

Identifying CAP patients who require ICU admission can be a difficult task, and a poor selection process can be disastrous. Indeed, previous studies reported that early ICU admission of patients with severe CAP is associated with a lower 28-day mortality and shorter length of stay than delayed ICU admission patients. These studies concluded that some patients without major criteria for severe CAP may benefit from early ICU admission [9-11].

Substantial variations in processes of care by gender according to have been shown for patients with cardiorespiratory diseases [12, 13]. Female patients with acute myocardial infarction and heart failure trend to receive poorer quality of care [14-16]. Kaplan et al found gender differences in the outcomes for CAP patients, with higher mortality for male patients [17]. To our knowledge, no study investigated whether these gender disparities reflected variations in processes of care rather than differences in baseline characteristics or diseases severity.

The aim of this study was to compare early ICU admission and outcomes for male and female inpatients hospitalized for CAP. We hypothesized that male patients were less likely to be early admitted to the ICU and yielded worse 28-day mortality.

Materials and Methods

Study Design

We performed a *post hoc* analysis of the original data from the Emergency Department Community-Acquired Pneumonia (EDCAP) and Pneumocom-1 studies. The methods used for both studies are reported elsewhere [10, 18]. Briefly, the EDCAP study was a cluster randomized trial involving 32 hospitals in Connecticut and western Pennsylvania, while the Pneumocom-1 study was a multicenter prospective observational cohort study conducted in 16 hospitals in France. Each study protocol received the approval from the institutional review boards at the participating institutions.

Patients

The EDCAP and Pneumocom-1 studies enrolled adult patients presenting to the emergency department (ED) with a clinical and radiographic diagnosis of CAP. The present analysis focused on inpatients, defined as patients admitted from the ED to a hospital ward or to a short-term ED monitoring unit for more than 24 h after initial presentation. To comply with the scope of CAP [19], we excluded nursing home residents and patients recently discharged from the hospital. Patients lost to follow-up or with missing data for ICU admission were also excluded from the analysis.

Data Collection

Baseline demographic characteristics, comorbid conditions, physical examination findings, laboratory test results, radiographic findings, and site of treatment were prospectively collected using physician interviews and structured chart reviews. We retrospectively computed the Pneumonia Severity Index (PSI) for each patient [6]. The PSI

comprises 20 clinical, laboratory, and X-ray parameters that are routinely available on ED presentation (Appendix 1). Missing values were assumed to be normal when computing the prediction scores. This is the same strategy as used for the original derivation and/or validation of the PSI.

ICU Admission and Timing

Consistent with previous studies [9], we defined patients admitted to ICU on the day of ED presentation as early ICU admissions, whereas we categorized those admitted to ICU more than 1 day after ED presentation as late ICU admissions. Patients who were not admitted to ICU during the index hospital stay were defined as non-ICU admissions. In both original studies, the decision to admit patients to ICU was at the discretion of the attending physician, and there were no specific recommendations regarding the indications or timing of ICU admission.

Outcome Measure

The main outcome measure was 28-day all-cause mortality. Follow-up clinical data were collected using structured chart reviews and telephone interviews with the patients, their relative, or their family physician at least 28 days after enrollment.

Statistical Analysis

We reported baseline patient characteristics as medians and interquartile ranges (IQR; i.e., 25th and 75th percentiles) for continuous variables and percentages for categorical variables. We compared baseline characteristics between male and female patients using the Kruskal-Wallis test for continuous variables and the chi-square test, or Fisher exact test where appropriate, for categorical variables.

We stratified our comparison of ICU admission by gender, across PSI risk class. We performed multinomial logistic regression for estimating the odds-like ratio (OR) of early and late ICU admission respectively for male relate to female patients. We used no ICU admission as reference. The covariates entered in the model included gender, PSI risk classes, and a first order interaction term between these two variables. We tested the interaction for significance. We plotted a forest plot depicting the OR of ICU admission for male relate female across PSI risk class and 95 % confidence intervals.

We developed a multivariable logistic regression model that estimated the OR of 28-day mortality for male relate female adjusted for ICU admission and PSI risk class. Because PSI risk class I perfectly predicted 28-day survival, we collapsed PSI risk class I and II into a single category, using as reference.

Two-sided *P* values of less than 0.05 were considered to be statistically significant. Analyses were performed using R version 3.0.1.

Results

Of the 4,216 patients enrolled in the two original studies, 1,968 patients were excluded from the present analysis (1,289 outpatients, 255 nursing home residents, 16 patients lost to follow-up and 8 patients with missing data for ICU admission). Our analytical sample consisted of 2,558 inpatients including 1,368 (53.5%) male patients and 1,190 female patients (46.5%) (Figure 1). The median age for all patients was 74 years (IQR, 59-81).

Comparison of Baseline Patients characteristics

The baseline characteristics stratified by gender are presented in Table 1. Male patients were more likely to have a comorbid condition (neoplastic disease, renal disease and coronary artery disease) but were less likely to have a chronic pulmonary disease. A greater proportion of men had preserved pulse oximetry, but men had higher rates of laboratory abnormalities (PaO₂<55mmHg, elevated blood urea nitrogen value). Overall, male patients were more likely to be assigned to PSI risk classes IV-V (53.6% vs. 37.3%) (Table 2).

Comparison of ICU admission and timing

Male patients had higher rates of early ICU admission (8.3% vs. 7.1%) and late ICU admission (6.7% vs. 4.5%) (Table 2). Interestingly, we observed a significant first order interaction between PSI risk class and gender for the odds of early and late relate to no ICU admission (p for interaction = 0.02) (Figure 2): compared with women, male patients assigned to PSI risk class V had a lower rate of early ICU admission (17% vs. 26%), which was compensated by a higher percentage of late ICU admission (10% vs. 2%) (Table 3). The interaction between gender and comorbid conditions, physical examination, laboratory and radiographic findings were not significant (Appendix)

Comparison of Mortality

Comparable 28-day mortality rates were observed for male and female patients (7.5% vs. 6.5%) (Table 2). In multivariable analysis adjusting for ICU admission and PSI, the odds ratio of mortality for male relate to female patients was 0.81 (95% confidence interval, 0.59 to 1.13). No significant interaction was found between gender and ICU admission for the odds of death (p for interaction = 0.24)

Discussion

This between-gender comparison of differences in ICU admission for CAP patients was performed in two large cohorts of in-hospitalized patients. We highlight significant differences between men related women in the selection by the physicians for the patients ICU admission. Indeed, male patients with severe CAP are less frequently hospitalized in ICU within the first 24 hours than female patients (17% vs. 26%, $p=0.04$). This difference of ICU admission persists after adjustment for illness severity. Consequently, our post hoc analysis suggests that male patients with CAP who require ICU admission, at times, are less correctly identified than female patients.

We also present new information on important variations in process of care by sex. Even though we did not found disparities for 28-day mortality, Kaplan et al. have shown that men with CAP were more likely to die than women, with a large cohort of 623,718 CAP patients [17]. However, it was not demonstrated if sex differences in mortality was due to biologic differences or to other factors, such as access of care [17, 20]. Our findings about the gender disparities of ICU admission can partly explain the higher mortality among male patients with CAP. Indeed, Restrepo et al. demonstrated that patients admitted late to the ICU with CAP have a significant increase in mortality compared with those admitted directly or within the first 24 h of presentation [9]. In addition, the transfer of patients with CAP who are first admitted to a hospital ward to the ICU for respiratory failure or septic shock is associated with increase mortality [21]. More generally, early intensive cares have a positive effect for patients with severe sepsis [22].

Interestingly enough, the severity of male patient's diseases seemed to be underestimated by physicians at their ED presentation. Indeed, if male patients with severe CAP were less frequently hospitalized in ICU in early admission, they were also more frequently admitted

late to the ICU compared to female patients (10% vs. 2%). This significant number of subsequent transfer of male patients who are first admitted to a hospital ward to the ICU could be explained by physiological differences between men and women. Some animal and human studies suggest that males are more likely to develop sepsis than females, and males with sepsis had higher risk of developing septic shock [23-25]. These gender-determined differences in response to infection might result in an increase number of late ICU admission for the male patients, but they could not explain the smaller number of early ICU admission. The decision regarding the ICU admission carries with it a number of important implications. Although some main criteria like mechanical ventilation and sepsis means immediate transfer to ICU, some other criteria are more complex to identify and may delay ICU admission [26]. Early identification of severe CAP that is not obvious on presentation, but will ultimately require ICU admission, remains a challenge for the physicians [27]. For these reasons, considerable research work has been undertaken to develop reliable prediction rules over the past two decades. These include the original American Thoracic Society (ATS) guidelines published in 1993 and revised version published in 2001; the confusion, urea, respiratory, blood pressure, and age >65 years (CURB plus); the PSI; and most recently the Risk of Early Admission to Intensive Care Unit (REA-ICU) index published in 2009 [6, 28-30]. Despite the clinical validation of these scores and recommendations, there are still huge differences about process of care of patients with CAP. Not enough progress has been achieved since 1997, when Fine et al. demonstrated that “physicians often rely on their subjective impressions of a patient’s clinical appearance in making the initial decision about site of care” [31]. Indeed, Dean et al. observed in 2012 a twofold difference in pneumonia hospitalization rates among ED physicians, unexplained by objective data [32]. Our post hoc analysis reinforces this finding, with the demonstration of gender differences in the ICU admission decision.

Limitations

The potential limitations of this post hoc analysis deserve mention. First, clinicians were not asked for the reasons for ICU admission because the original studies were not designed for that purpose. Additionally, clinician's baseline characteristics were not collected. Future prospective studies are needed to document physician reasons for early or late ICU admission of patients with severe CAP and their characteristics to improve understanding of the root causes of their subjective impressions and the origin of the gender bias.

Second, ICU admission was not based on random assignment in this study and the results may be confounded by differences in patient characteristics. Although our adjustment for severity illness eliminated all significant imbalances observed between male and women patients, unmeasured baseline characteristics, organizational constraints such as bed availability, or process of care that we did not account for may exist and could explain these findings.

Third, the multinomial model was adjusted for severity illness, by using the PSI. The PSI was a prognostic model that was originally developed to identify patients who could be managed at home, and have limited ability to predict ICU admission. However, even though other prediction rules were validated, PSI remains the reference to class and discriminate the severity degrees of CAP, taking into account common severity criteria to other scores.

Fourth, our analysis was limited by data collected in the two original studies, and certain severity criteria were not measured, such as albumin, serum lactate, and platelet counts. However, all data were prospectively gathered using case report forms, thereby maximizing data reliability and minimizing missing values.

Fifth, our study did not account for patients with “do not resuscitation” status. This could contribute to overestimating the short-term mortality rate for patients not admitted to the ICU [33], although admission for palliative care was an exclusion in the EDCAP trial.

Conclusions

Our findings suggest that female patients with severe CAP who require ICU admission are better identified than male patients. These findings contribute to our understanding of the potential higher mortality of male patients with CAP and emphasize the need for better and earlier identification of patients will ultimately require ICU admission, based on objective criteria. Further research is warranted to refine the concept of severe community-acquired pneumonia to guide the initial decision on the site of care for inpatients. In addition with previous studies, our findings suggest that male inpatients with CAP have a poorer quality of care related to female patients. These results are opposite to those for cardio respiratory diseases, which show that female patients trend to receive poorer quality of care. Furthermore, it seems essential to better understand the mechanisms underlying the observed gender disparities, before to conclude to the existence of a sex inequality in process of care. Alongside the development of prediction rules, it would be interesting to assess the representation of gender among physicians and patient's families.

THESE SOUTENUE PAR : M. BOUSSAT Bastien

TITRE: GENDER DIFFERENCES IN EARLY VERSUS LATE INTENSIVE CARE UNIT ADMISSION FOR COMMUNITY-ACQUIRED PNEUMONIA PATIENTS.

CONCLUSION

Le Pneumonie aiguë communautaire (PAC) est la sixième cause de décès dans le monde. Le taux de mortalité des patients hospitalisés pour une PAC est d'environ 5%, et leur taux d'admission en réanimation durant leur séjour varie entre 4 et 19% dans la littérature. Il a été précédemment démontré que pour les patients les plus sévères, une admission en réanimation dans les 24 premières heures de l'hospitalisation était associée à une réduction de la mortalité à 28 jours et de la durée moyenne de séjour, par rapport à une admission retardée.

Il a été suggéré que le pronostic de la PAC était plus défavorable chez les hommes que chez les femmes, notamment en termes de mortalité. On ignore cependant si ces différences sont liées à des variations dans la prise en charge ou dans les caractéristiques initiales des patients (comorbidités, sévérité).

A partir des données des études de cohorte prospectives multicentriques EDCAP (Etats-Unis) et Pneumocom-1 (France), nous avons mis en évidence que les hommes atteints de PAC sévère (classe V du Pneumonia Severity Index) étaient moins fréquemment admis en réanimation lors des 24 premières heures de l'hospitalisation (17% vs. 26%), et plus souvent admis tardivement (10% vs. 2%), comparativement aux femmes (p d'interaction = 0.02).

Cette étude démontre que les hommes atteints d'une PAC sévère sont admis plus tardivement en réanimation que les femmes et suggère l'existence d'un biais sexiste en faveur des femmes dans la prise en charge des patients atteints de PAC.

VU ET PERMIS D'IMPRIMER

Grenoble, le 15/3/2014

LE DOYEN


J.P. ROMANET


LE PRESIDENT DE LA THESE


P.FRANÇOIS

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Tables and Figures

Table 1. Comparison of Patient Baseline Characteristics between male and female CAP patients

Characteristics	All patients		Male		Female		<i>P</i> -value
	<i>n</i>	(%)	<i>n</i>	(%)	<i>n</i>	(%)	
Age, median (IQR), y	74	(59–81)	73	(59–81)	74	(60–83)	0.06
Comorbid conditions, <i>n</i> (%)							
Neoplastic disease	163	(6.4)	108	(7.9)	55	(4.6)	< 0.001
Liver disease	34	(1.3)	20	(1.5)	14	(1.2)	0.53
Congestive heart failure	464	(18.1)	257	(18.8)	207	(17.4)	0.36
Renal disease	198	(7.7)	131	(9.6)	67	(5.6)	< 0.001
Coronary artery disease	618	(24.2)	387	(28.3)	231	(19.4)	< 0.001
Chronic pulmonary disease	861	(33.7)	428	(31.3)	433	(36.4)	0.006
Cerebrovascular disease	237	(9.3)	141	(10.3)	96	(8.1)	0.051
Diabetes mellitus	547	(21.4)	298	(21.8)	249	(20.9)	0.59

Table 1. Comparison of Patient Baseline Characteristics between male and female CAP patients (continued)

Characteristics	All patients (<i>n</i> =2,558)		Male (<i>n</i> =1,368)		Female (<i>n</i> =1,190)		<i>P</i> -value
Physical examination findings, <i>n</i> (%)							
Altered mental status	232	(9.1)	128	(9.4)	104	(8.7)	0.58
Respiratory rate \geq 30 per min	463	(18.1)	264	(19.3)	199	(16.7)	0.09
Pulse rate \geq 130 per min	214	(8.4)	105	(7.7)	109	(9.2)	0.17
Systolic BP < 90 mmHg	58	(2.3)	29	(2.1)	29	(2.4)	0.59
Temperature < 36°C	99	(3.9)	55	(4.0)	44	(3.7)	0.67
Pulse oximetry < 90%	646	(25.2)	318	(23.2)	328	(27.6)	0.01
Laboratory and radiographic findings, <i>n</i> (%)							
Arterial pH < 7.40	213	(8.3)	115	(8.4)	98	(8.2)	0.87
PaO ₂ < 55 mmHg	248	(9.7)	151	(11.0)	97	(8.2)	0.01
BUN \geq 11 mmol/L	505	(19.7)	305	(22.3)	200	(16.8)	< 0.001
Sodium < 130 mEq/L	163	(6.4)	82	(6.0)	81	(6.8)	0.40
Glucose \geq 20 mmol/dL	51	(2.0)	31	(2.3)	20	(1.7)	0.29
Hematocrit < 30 %	173	(6.8)	95	(6.9)	78	(6.6)	0.70

Table 1. Comparison of Patient Baseline Characteristics between male and female CAP patients (continued)

Characteristics	All patients		Male		Female		<i>P</i> -value
	<i>n</i>	(%)	<i>n</i>	(%)	<i>n</i>	(%)	
WBC count < 4 giga/L	38	(1.5)	20	(1.5)	18	(1.5)	0.91
Multilobar infiltrates	623	(24.3)	336	(24.6)	287	(24.1)	0.80
Pleural effusion	452	(17.7)	248	(18.1)	204	(17.1)	0.51
Pneumonia Severity Index, <i>n</i> (%)							< 0.001
Class I	210	(8.2)	120	(8.8)	90	(7.6)	
Class II	501	(19.6)	172	(12.6)	329	(27.6)	
Class III	670	(26.2)	343	(25.1)	327	(27.5)	
Class IV	932	(36.4)	570	(41.7)	362	(30.4)	
Class V	245	(9.6)	163	(11.9)	82	(6.9)	

Abbreviations: BP, blood pressure; BUN, blood urea nitrogen; PaO₂, partial pressure of oxygen in arterial blood gas analysis;

WBC, white blood cell; IQR, interquartile range (i.e., 25th and 75th percentiles).

Table 2. Comparison of ICU admission and 28-day mortality by gender

	All patients (<i>n</i> =2558)		Male (<i>n</i> =1368)		Female (<i>n</i> =1190)		<i>P</i> -value
ICU admission, <i>n</i> (%)							0.02
No ICU admission	2215	(86.6)	1163	(85.0)	1052	(88.4)	
Early ICU admission ^a	199	(7.8)	114	(8.3)	85	(7.1)	
Late ICU admission ^b	144	(5.6)	91	(6.7)	53	(4.5)	
28-day mortality <i>n</i> (%)	200	(7.8)	103	(7.5)	77	(6.5)	0.30

^a Early ICU admission refers to patients who were transferred to the ICU on the same day as emergency department presentation.

^b Late ICU admission refers to patients who were transferred to the ICU after first being admitted to the medical ward for 1 day or more.

Table 3. Comparison of ICU admission between Male and Female patients with CAP stratified according to PSI risk classes (p = 0.02 for global interaction)

	No Admission		Early Admission		Late Admission		P-value
Class I							0.40
Male	110	(91.7)	5	(4.2)	5	(4.2)	
Female	84	(93.3)	1	(1.1)	5	(5.6)	
Class II							0.01
Male	148	(86.0)	14	(8.1)	10	(5.8)	
Female	309	(93.9)	11	(3.3)	9	(2.7)	
Class III							0.59
Male	307	(89.5)	18	(5.2)	18	(5.2)	
Female	296	(90.5)	12	(3.7)	19	(5.8)	
Class IV							0.22
Male	481	(84.4)	48	(8.4)	41	(7.2)	
Female	305	(84.3)	39	(10.8)	18	(5.0)	
Class V							0.04
Male	117	(71.8)	29	(17.8)	17	(10.4)	
Female	58	(70.7)	22	(26.8)	2	(2.4)	

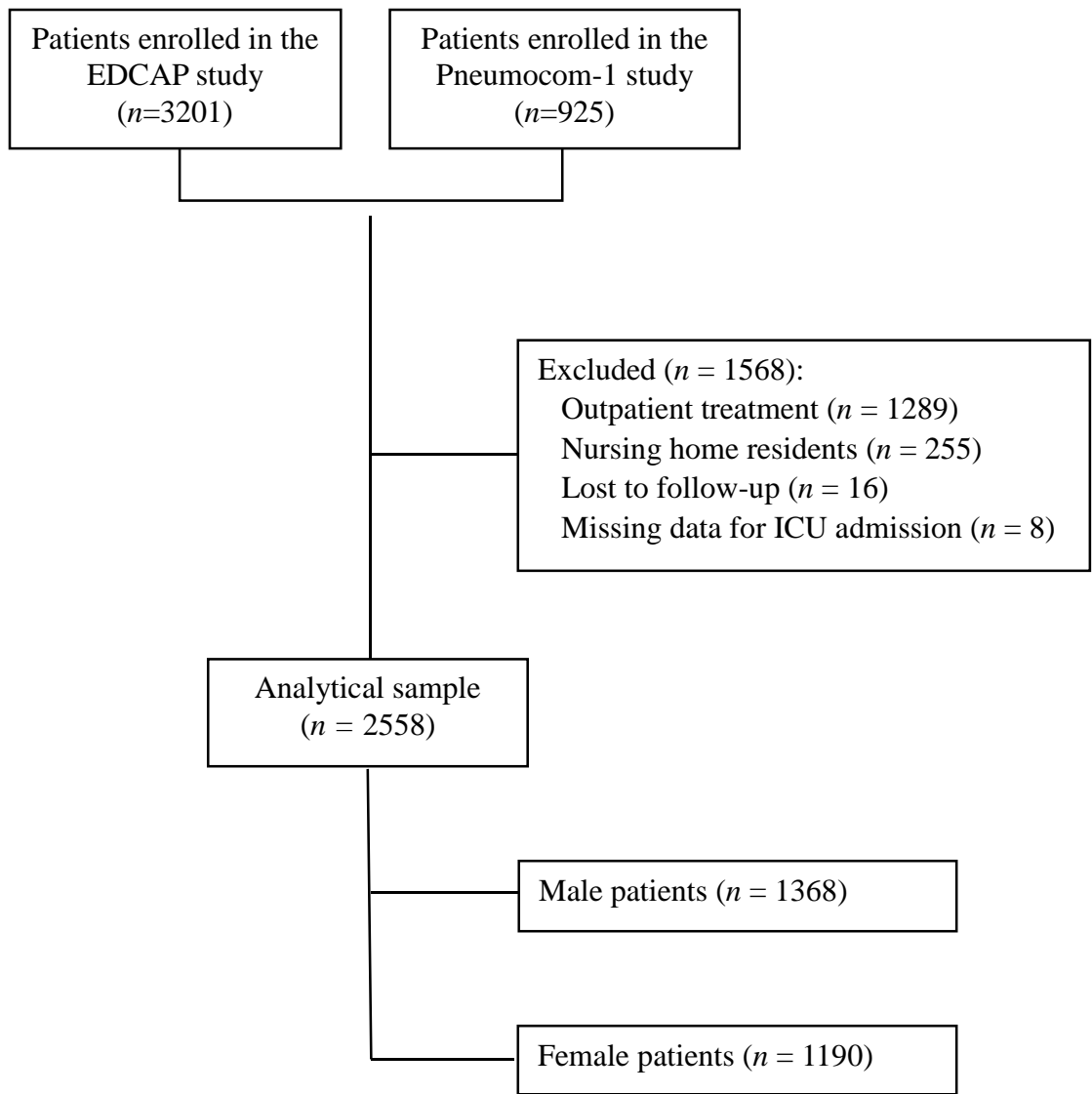
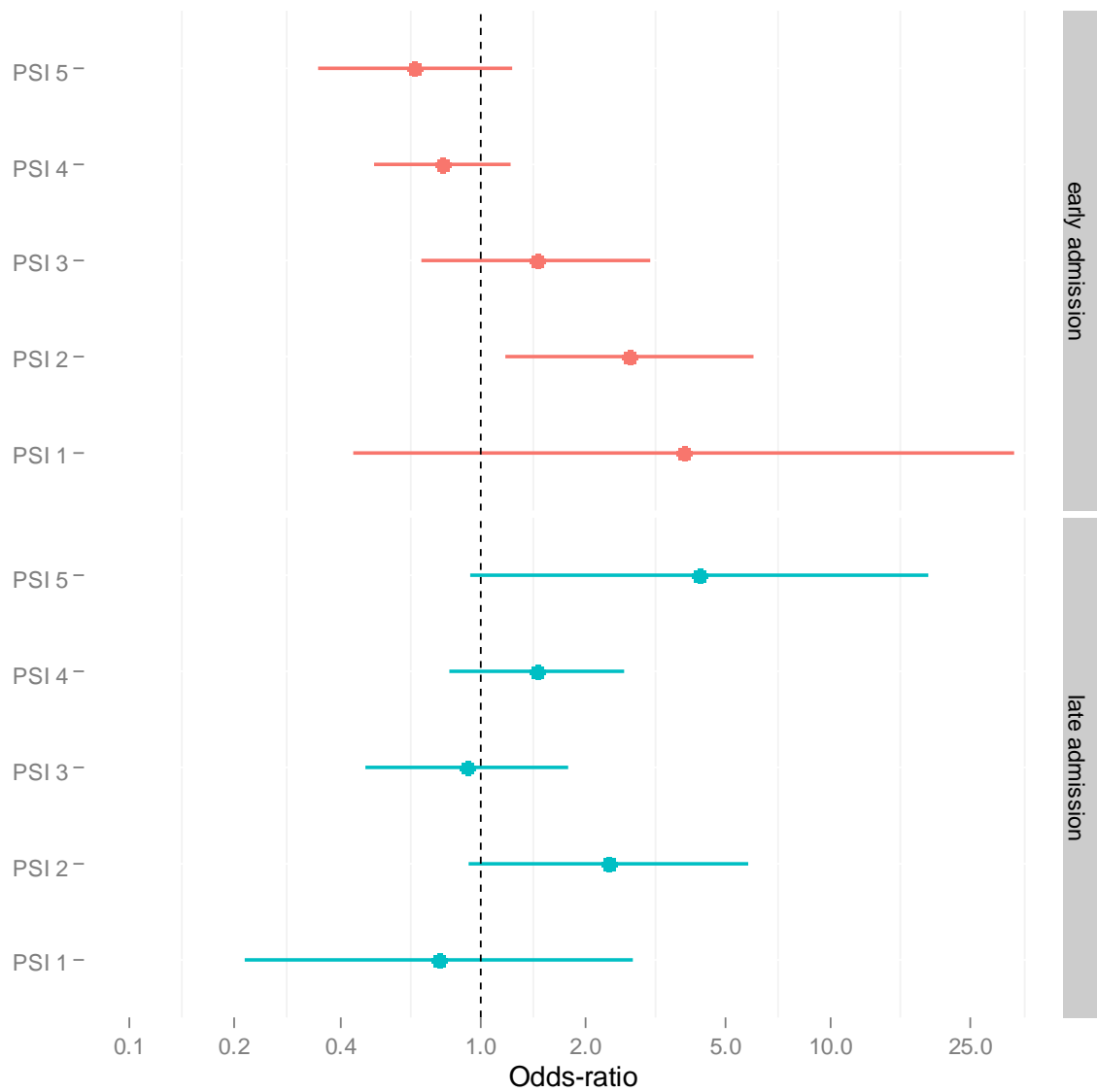


Figure 1: Patient enrollment

Figure 2. Odds like ratio of early and late ICU admission for male relate to female patients, no ICU admission as reference (p global for interaction = 0.020)



Appendix

Appendix 1. Pneumonia Severity Index⁸

Characteristics	Points	Risk class	Score
Age for men	age	I	-*
Age for women	age-10	II	≤ 70
Nursing home resident	10	III	71 to 90
Neoplastic disease	30	IV	91 to 130
Liver disease	20	V	> 130
Congestive heart failure	10		
Cerebrovascular disease	10		
Renal disease	10		
Altered mental status	20		
Respiratory rate ≥ 30/min	20		
Systolic BP < 90 mmHg	20		
Temperature < 35 or ≥ 40°C	15		
Pulse rate ≥ 125/min	10		
Arterial pH < 7.35	30		
BUN ≥ 30 mg/dL	20		
Sodium < 130 mEq/L	20		
Glucose ≥ 14 mmol/dL	10		
Hematocrit < 30%	10		
PaO ₂ < 60 mmHg (or SpO ₂ < 90%)	10		
Pleural effusion	10		

Abbreviations: BP, blood pressure; BUN, blood urea nitrogen; CAP, community-acquired pneumonia; CXR, chest radiography; FiO₂, fraction of inspired oxygen; ICU, intensive care unit; IDSA/ATS, Infectious Disease Society of America / American Thoracic Society; IRVS, intensive respiratory or vasopressor support; PaO₂, partial pressure of arterial oxygen; REA-ICU, risk of early admission to the intensive care unit; SpO₂, pulse oximetric saturation; WBC, white blood cell.

* Assignment to PSI risk class I was determined by the absence of all predictors among age > 50 years, neoplastic disease, congestive heart failure, cerebrovascular disease, renal disease, liver disease, altered mental status, pulse rate ≥ 125/min, respiratory rate ≥ 30/min, systolic blood pressure < 90 mmHg, and temperature < 35 or ≥ 40°C.

Appendix 2. Comparison of ICU admission between Male and Female patients with CAP stratified according to comorbid conditions, physical examination standing, laboratory and radiographic findings

Characteristics	Male			Female			P*
	N (n=1163)	E (n=114)	L (n=91)	N (n=1052)	E (n=85)	L (n=53)	
Age > 65 y	800 (68,8)	66 (57,9)	64 (70,3)	740 (70,3)	58 (68,2)	30 (56,6)	0,08
Comorbid conditions, <i>n</i> (%)							
Neoplastic disease	90 (7,7)	11 (9,6)	7 (7,7)	50 (4,8)	4 (4,7)	1 (1,9)	0,60
Liver disease	16 (1,4)	3 (2,6)	1 (1,1)	13 (1,2)	0 (0,0)	1 (1,9)	0,20
Congestive heart failure	208 (17,9)	29 (25,4)	20 (22,0)	174 (16,5)	18 (21,2)	15 (28,3)	0,51
Renal disease	103 (8,9)	13 (11,4)	15 (16,5)	50 (4,8)	12 (14,1)	5 (9,4)	0,15
Coronary artery disease	334 (28,7)	28 (24,6)	25 (27,5)	201 (19,1)	21 (24,7)	9 (17,0)	0,29
Chronic pulmonary disease	366 (31,5)	40 (35,1)	22 (24,2)	377 (35,8)	39 (45,9)	17 (32,1)	0,64
Cerebrovascular disease	124 (10,7)	7 (6,1)	10 (11,0)	86 (8,2)	6 (7,1)	4 (7,5)	0,74
Diabetes mellitus	248 (21,3)	22 (19,3)	28 (30,8)	213 (20,2)	20 (23,5)	16 (30,2)	0,68

N: No ICU admission E: Early ICU admission L: Late ICU admission p*: p for interaction

Comparison of ICU admission between Male and Female patients with CAP stratified according to comorbid conditions, physical examination standing, laboratory and radiographic findings (continued)

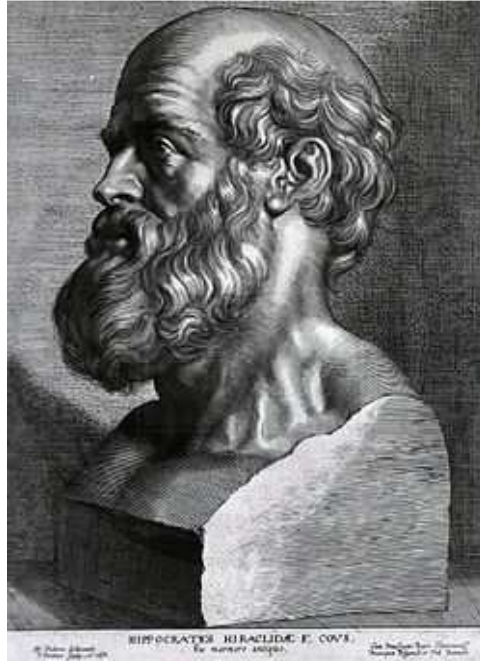
Characteristics	Male						Female						<i>p</i> *
	N (n=1163)		E (n=114)		L (n=91)		N (n=1052)		E (n=85)		L (n=53)		
Physical examination findings, <i>n</i> (%)													
Altered mental status	97	(8,3)	21	(18,4)	10	(11,0)	73	(6,9)	23	(27,1)	8	(15,1)	0,13
Respiratory rate \geq 30 per min	198	(17,0)	47	(41,2)	19	(20,9)	160	(15,2)	28	(32,9)	11	(20,8)	0,74
Pulse rate \geq 130 per min	74	(6,4)	23	(20,2)	8	(8,8)	93	(8,8)	12	(14,1)	4	(7,5)	0,14
Systolic BP < 90 mmHg	23	(2,0)	5	(4,4)	1	(1,1)	19	(1,8)	7	(8,2)	3	(5,7)	0,18
Temperature < 36°C	45	(3,9)	7	(6,1)	3	(3,3)	38	(3,6)	3	(3,5)	3	(5,7)	0,57
Pulse oximetry < 90%	238	(20,5)	55	(48,2)	25	(27,5)	266	(25,3)	41	(48,2)	21	(39,6)	0,48

N: No ICU admission E: Early ICU admission L: Late ICU admission *p**: *p* for interaction

Comparison of ICU admission between Male and Female patients with CAP stratified according to comorbid conditions, physical examination standing, laboratory and radiographic findings (continued)

Characteristics	Male						Female						P*
	N (n=1163)		E (n=114)		L (n=91)		N (n=1052)		E (n=85)		L (n=53)		
Laboratory and radiographic findings, n (%)													
Arterial pH < 7.40	81	(7,0)	29	(25,4)	5	(5,5)	58	(5,5)	37	(43,5)	3	(5,7)	0,01
PaO ₂ < 55 mmHg	106	(9,1)	35	(30,7)	10	(11,0)	78	(7,4)	16	(18,8)	3	(5,7)	0,43
BUN ≥ 11 mmol/L	233	(20,0)	39	(34,2)	33	(36,3)	152	(14,4)	33	(38,8)	15	(28,3)	0,18
Sodium < 130 mEq/L	63	(5,4)	10	(8,8)	9	(9,9)	62	(5,9)	15	(17,6)	4	(7,5)	0,23
Glucose ≥ 20 mmol/dL	24	(2,1)	4	(3,5)	3	(3,3)	11	(1,0)	5	(5,9)	4	(7,5)	0,09
Hematocrit < 30 %	74	(6,4)	8	(7,0)	13	(14,3)	63	(6,0)	11	(12,9)	4	(7,5)	0,17
WBC count < 4 giga/L	17	(1,5)	3	(2,6)	0	(0,0)	13	(1,2)	3	(3,5)	2	(3,8)	0,11
Multilobar infiltrates	260	(22,4)	47	(41,2)	29	(31,9)	237	(22,5)	33	(38,8)	17	(32,1)	0,94
Pleural effusion	200	(17,2)	22	(19,3)	26	(28,6)	173	(16,4)	19	(22,4)	12	(22,6)	0,64

N: No ICU admission E: Early ICU admission L: Late ICU admission p*: p for interaction



Serment d'Hippocrate

En présence des Maîtres de cette Faculté, de mes chers condisciples et devant l'effigie d'HIPPOCRATE,

Je promets et je jure d'être fidèle aux lois de l'honneur et de la probité dans l'exercice de la Médecine.

Je donnerais mes soins gratuitement à l'indigent et n'exigerai jamais un salaire au dessus de mon travail. Je ne participerai à aucun partage clandestin d'honoraires.

Admis dans l'intimité des maisons, mes yeux n'y verront pas ce qui s'y passe ; ma langue taira les secrets qui me seront confiés et mon état ne servira pas à corrompre les moeurs, ni à favoriser le crime.

Je ne permettrai pas que des considérations de religion, de nation, de race, de parti ou de classe sociale viennent s'interposer entre mon devoir et mon patient.

Je garderai le respect absolu de la vie humaine.

Même sous la menace, je n'admettrai pas de faire usage de mes connaissances médicales contre les lois de l'humanité.

Respectueux et reconnaissant envers mes Maîtres, je rendrai à leurs enfants l'instruction que j'ai reçue de leurs pères.

Que les hommes m'accordent leur estime si je suis fidèle à mes promesses.

Que je sois couvert d'opprobre et méprisé de mes confrères si j'y manque.