








Original Article

Factors Affecting Cost of Patients with Severe Community-Acquired Pneumonia in Intensive Care Unit

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Abstract

OBJECTIVES: The aim of this study is to investigate the factors affecting cost in patients with severe community-acquired pneumonia (CAP) who were admitted to the intensive care unit (ICU).

MATERIALS AND METHODS: This retrospective cohort study was conducted between January 2013 and December 2016. A total of 291 sequential patients with severe CAP were included in the study. Patients' demographic and clinical data; the need for invasive mechanical ventilation or non-invasive mechanical ventilation; intensive care severity (ICU) scores, including Acute Physiology and Chronic Health Evaluation (APACHE II), Sepsis-related Organ Failure Assessment, Quick SOFA, pneumonia severity index (PSI); and Confusion, Urea, Respiratory Rate, and Blood Pressure-65 (CURB-65) scores were obtained from medical records and recorded for all cases.

RESULTS: The mean age of 291 patients was 68.4±16.8 years, and 61% were female. The median length of ICU stay was 7 days. Forty-six percent of patients had chronic obstructive pulmonary disease (COPD), and 42% had hypertension. The mean cost of each hospitalization was US\$ 2722 (TL 5578). The highest cost was found in the group of patients aged 50–59 years, and the lowest cost was found in the patients aged <50 years. A statistically significant relationship was found between ICU severity scores and health cost. The cost of patients in PSI class V, APACHE II (>20 points), and CURB-65 score were higher. The presence of COPD, atrial fibrillation, congestive heart failure, hypoalbuminemia, mental state deterioration, in-hospital mortality, severe sepsis, septic shock, mechanical ventilation requirement, and haloperidol and vasopressor usage were associated with higher cost, while the use of florokinolon was associated with lower cost.

CONCLUSION: The presence of certain comorbidities and high disease severity in patients with severe CAP hospitalized in ICU increase the cost of inpatient treatment. The need for mechanical ventilation during treatment and the presence of sepsis/septic shock are additional factors that increase the cost.

KEYWORDS: Cost, drug use, intensive care, severe community-acquired pneumonia

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INTRODUCTION

Community-acquired pneumonia (CAP) is a disease that can be treated in government and private health institutions, polyclinics, emergency services, and inpatient facilities, and treatment costs are high [1]. Severe pneumonia criteria are defined as acute respiratory insufficiency findings (respiration rate >30/min and PaO₂/FiO₂ <250); severe sepsis–septic shock findings (hypotension, i.e., systolic blood pressure <90 mmHg and diastolic blood pressure <60 mmHg, along with kidney insufficiency and confusion); and extensive infiltration (multilobar or bilateral infiltration) [2].

In a single-centered study published in Turkey, the mortality rate in patients diagnosed with CAP and treated in intensive care units (ICUs) has been found at 52% [3]. Pneumonia in patients aged >65 years accompanied by chronic obstructive pulmonary disease (COPD), malignancy, diabetes mellitus, chronic kidney insufficiency, congestive heart failure (CHF), or chronic liver disease is reported to progress relatively more frequently and severely [4]. Of patients with severe CAP, 60%–90% need mechanical ventilation support. The average hospitalization of patients with severe CAP in need of mechanical ventilation lasts 16 days [2]. Failure to comply with clinical guides' suggestions during choosing antibiotics in treatment of severe CAP has been reported to extend the duration of mechanical ventilation by 3 days and increase costs [4]. Choosing an appropriate antibiotic during the management of CAP reduces clinical failure, multiple drug usage, development of resistance, and treatment cost significantly [5]. CAP has great importance in terms of economics since it is very frequently observed. Early mobilization of inpatients decreases hospitalization duration and reduces cost [6]. The immediate diagnosis after hospitalization and early start of treatment are important factors in terms of cost, prognosis, and mortality.

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It has been reported that the application of antibiotics within 4h of hospitalization reduces the length of stay in the hospital, whereas a delay of the application of antibiotics >8 h increases mortality [7]. Additional illnesses, mainly COPD, have been reported in varying ratios of 1/3–1/2 in patients with CAP [8]. This ratio can increase up to 80% in patients with CAP who require intensive care [8]. The most frequent comorbidity has been reported as COPD (22%–31%) [9, 10]. Comorbid situations increase hospital costs. To the best of our knowledge, there has been no comprehensive study regarding the expense of patients with severe Turkish CAP monitored in the ICU. The aim of the present study was to investigate the cost and the factors that influence it in patients with severe CAP treated in ICUs.

MATERIAL AND METHODS

This was a retrospective multicentered cohort study aimed to determine the hospitalization costs and factors that affect the expenses, which included 291 consecutive patients with severe CAP (University of Health Sciences Süreyyapaşa Chest Diseases and Thoracic Surgery Training and Research Hospital, Dokuz Eylül University School of Medicine, Ankara University School of Medicine, Akdeniz University School of Medicine) between January 2013 and December 2016. Patients included in the study were composed of cases who had been accepted to the ICU after the emergency service and other services. Demographic properties and clinical findings were obtained after scanning of epicrisis and 4-year medical records of all cases. The age of the patients, gender, length of stay in the ICU, clinical and laboratory findings, medications, comorbidities, applications of invasive mechanical ventilation (IMV), and non-invasive mechanical ventilation (NIMV), and intensive care severity reports, such as Acute Physiology and Chronic Health Evaluation (APACHE) II [11], Sepsis-related Organ Failure Assessment (SOFA) [12], quick SOFA [13], Pneumonia Severity Index (PSI) [14], and Confusion, Urea, Respiratory Rate, and Blood Pressure-65 (CURB-65) [15], scores, have been recorded. In addition, the total outcome in the ICU (e.g., examination fees, treatment service fees, bed fees, and medication and consumable fees) was recorded. The expense for each patient in dollars was calculated on the date when patients were admitted to ICUs.

Specifications/Definitions

Suspected CAP definition

Acute disease with at least one of the symptoms of new focal pulmonary diseases and coughing, fever lasting >4 days, or the occurrence of dyspnea/tachypnea and symptoms without specific explanatory reasons [16].

Definite CAP definition

In addition to the abovementioned, the presence of possibly new positive symptoms in lung X-ray. In the elderly, those were symptoms in lung X-ray accompanying the acute clinical disease (unspecified) without a definite reason [16].

Hospital cost calculation

It is calculated by considering the SSI (Social Security Institution) payments at the time when patients were placed in ICUs according to SSI Level 3 costs.

Immunosuppressive diseases

Patients with human immunodeficiency virus infection, who had used high doses of immunosuppressive drugs for a long time, patients with cancer, those who developed pneumonia 48 h after being placed in ICU, and those whose pulmonary symptoms and radiological findings (e.g., pulmonary fluid retention, pulmonary emboli, and lung carcinoma) could be explained by alternative diagnosis were excluded from the study.

The study was approved by the Akdeniz University Ethical Committee (January 17, 2018; decision no: 48). It was conducted in accordance with the Declaration of Helsinki.

Statistical Analysis

Data were analyzed using the Statistical Package for the Social Sciences version 21.0 package program (SPSS IBM Corp.; Armonk, NY, USA) for statistical analysis. In the case of nor-

Table 1. Clinical properties of 291 patients observed in the intensive care unit due to severe CAP

Variables	All patients (n=291)
Gender	
Male, n (%)	113 (38.8)
Female, n (%)	178 (61.2)
Age, year	68.4±16.8
Cost, TL	5578.5052
Cost, US\$	2721.9485
Hospitalization	
Average ± SD, day	9.8±12.2
Median (IQR), day	7 (4–11)
APACHE II	21.8±7.8
SOFA	5.8±3.0
PaO ₂ /FiO ₂	191.2±85.8
Additional conditions, n (%)	
COPD	133 (45.7)
DM	67 (23)
AF	43 (14.8)
HT	123 (42.3)
CKI	24 (8.2)
CLI	7 (2.4)
CVE	35 (12)
HL	13 (4.5)
CAD	45 (15.5)
Arrhythmia	22 (7.6)
CHF	73 (25.1)
VD	9 (3.1)

Data are expressed as average±standard deviation or n (%)
 APACHE: acute physiology and chronic health evaluation; SOFA: sepsis-related organ failure assessment; IQR: interquartile range; COPD: chronic obstructive pulmonary disease; DM: diabetes mellitus; AF: atrial fibrillation; HT: hypertension; CKI: chronic kidney insufficiency; CLI: chronic liver insufficiency; CVE: cerebrovascular event; HL: hyperlipidemia; CAD: coronary artery disease; CHF: congestive heart failure; VD: valve disease

Table 2. Cost investigation of patients with severe CAP in the intensive care unit

Variables		Cost (TL) Median (Q.1–Q.3)	p
Gender			
Female (n=113)		3459 (1710–5024)	0.57
Male (n=178)		3269 (2001–6095)	
Age			
(n=39)	<50 years	2040 (1308–3008)	
(n=21)	50–59 years	4281 (3426–6628)	<0.001
(n=73)	60–69 years	3964 (2429–5296)	
(n=73)	70–79 years	3766 (2195–7767)	
(n=85)	>80 years	3121 (1618–5273)	
COPD	No (n=158)	3086 (1523–4921)	0.009
	Yes (n=133)	4040 (2332–6424)	
DM	No (n=224)	3354 (1825–5748)	0.91
	Yes (n=67)	3342 (1999–5296)	
AF	No (n=248)	3231 (1653–5285)	0.046
	Yes (n=43)	3893 (2808–6985)	
HT	No (n=168)	3191 (1828–5285)	0.42
	Yes (n=123)	3717 (1957–6269)	
CKI	No (n=267)	3391 (1957–5296)	0.75
	Yes (n=24)	3125 (1605–9078)	
CLD	No (n=284)	3293 (1883–5399)	0.39
	Yes (n=7)	4910 (3002–6402)	
CVE	No (n=256)	3420 (1990–6099)	0.16
	Yes (n=35)	3103 (1592–4373)	
HL	No (n=278)	3344 (1893–5667)	0.76
	Yes (n=13)	3342 (2467–4260)	
CAD	No (n=246)	3232 (1776–5159)	0.11
	Yes (n=45)	4040 (2305–6740)	
Arrhythmia	No (n=269)	3342 (1832–5273)	0.17
	Yes (n=22)	3378 (3069–7525)	
CHF	No (n=218)	3120 (1641–5151)	0.042
	Yes (n=73)	4040 (2433–6424)	
VD	No (n=282)	3320 (1957–5417)	0.78
	Yes (n=9)	4185 (1309–7525)	
Hypoalbuminemia <3.5 g/dL	No (n=58)	3039 (2138–4540)	0.001
	Yes (n=233)	3424 (1776–5829)	
pH <7.35 or >7.35	Alkaline (n=118)	2536 (1576–4921)	0.47
	Acidic (n=173)	4020 (2406–6426)	
Mental status disorder	No (n=174)	3129 (1710–4780)	0.013
	Yes (n=117)	4040 (2195–7004)	
Septic shock	No (n=172)	2648 (1480–4026)	<0.001
	Yes (n=119)	4924 (3002–8524)	
Severe sepsis	No (n=86)	2508 (1391–4088)	<0.001
	Yes (n=205)	3858 (2245–6628)	
IMV necessity	No (n=138)	2398 (1470–3490)	<0.001
	Yes (n=153)	4768 (3002–8360)	
NIMV necessity	No (n=103)	2269 (1157–4373)	<0.001

Table 2. Cost investigation of patients with severe CAP in the intensive care unit (continued)

Variables		Cost (TL) Median (Q.1–Q.3)	p
Beta-lactam usage	Yes (n=188)	3946 (2472–6683)	0.17
	No (n=234)	3231 (1832–5159)	
Beta-lactam+macrolide usage	Yes (n=57)	3964 (2245–6974)	0.15
	No (n=255)	3276 (1957–5159)	
Beta-lactam+fluoroquinolone usage	Yes (n=36)	4445 (1756–9074)	0.07
	No (n=152)	3163 (1636–4803)	
Fluoroquinolone usage	Yes (n=139)	3717 (2195–6095)	0.033
	No (n=205)	3558 (2103–6628)	
Haloperidol usage	Yes (n=86)	3151 (1667–4290)	<0.001
	No (n=233)	3113 (1633–4690)	
Vasopressor usage	Yes (n=58)	6261 (3201–11,576)	<0.001
	No (n=162)	2559 (1470–3766)	
	Yes (n=129)	4910 (3002–8524)	

Q: quartile; COPD: chronic obstructive pulmonary disease; DM: diabetes mellitus; AF: atrial fibrillation; HT: hypertension; CKI: chronic kidney insufficiency; CLD: chronic liver disease; CVE: cerebrovascular event; HL: hyperlipidemia; CAD: coronary artery disease; CHF: congestive heart failure; VD: valve disease; IMV: invasive mechanical ventilation; NIMV: non-invasive mechanical ventilation

mal or non-normal distributions, continuous numerical data were expressed as the average \pm standard deviation or 25%–75% median, respectively. Categorical data, such as gender and IMV/NIMV applications, were expressed as numbers and percentages. In the comparison of continuous numerical variables with irregular distribution in independent groups, the Mann–Whitney U test was used in the case of two groups, whereas the Kruskal–Wallis test was used in the presence of more than two groups. For comparison between the groups, chi-squared test (χ^2) was used in the evaluation of two independent groups. The correlation between PaO₂/FiO₂ values and cost has been evaluated by Spearman's correlation test. A p-value <0.05 was considered to be statistically significant. In a multivariable logistic regression analysis, as dependent variable, cost variables below and above the median value were used and intended to detect independent variants that predict the cost being higher than the median (TL 2932.00) calculated in the present study. A logistic regression analysis (backward method) was run using factors affecting the potential cost obtained in a single variable analysis together with other variables found and predicted to be found statistically significant in other studies.

RESULTS

A total of 291 consecutive patients with CAP hospitalized in adult ICUs in a 4-year retrospective period were included in the study. Demographic findings of all patients, clinical features, and total expenses are presented in Table 1. The comparison of patients in terms of treatment expenses are presented in Table 2.

In patients with severe CAP aged 50–59 years, the cost was found to be significantly high (p<0.001). Statistically significant correlations were detected between COPD (p=0.009), atrial fibrillation (AF; p=0.046), CHF (p=0.042), hypoalbuminemia (p=0.001), severe sepsis (p<0.001), septic shock (p<0.001), and IMV and NIMV applications (p<0.001), and

applications of haloperidol and vasopressor and costs. The expenses were significantly lower in patients who only used fluoroquinolone (p=0.033). Isolated use of fluoroquinolones was also associated with reduced mortality (p=0.009). Expenses were significantly higher in patients with severe CAP accompanied by confusion (p=0.013).

When the relationships between the PSI risk class, APACHE II score, CURB-65 score, SOFA and quick SOFA scores, and expenses were investigated, a statistically significant difference was detected between the PSI risk class, APACHE II score, CURB-65 score, and costs (p=0.001, p=0.001, and p=0.009, respectively). Expenses were higher in patients who were in the PSI Group V, who had an APACHE II score >20 points, and who had a CURB-65 score \geq 3 points. The correlation between the PSI, APACHE II, CURB-65, SOFA, and quick SOFA scores, and expenses in patients with severe CAP is shown in Table 3. The results of the logistic regression analysis performed to detect the factors affecting the hospitalization expenses being higher than the median calculated in our patient cohort (2932.00 TL) are shown in Table 4. In this respect, in patients with severe CAP, the use of IMV and NIMV, the applications of haloperidol or vasopressors, PSI Group V, and severe sepsis findings were detected as independent variants determining an increase in ICU expenses. The age <50 years was found to be correlated with low hospitalization expenses.

DISCUSSION

In the present study, the hospitalization expenses and factors that affect the cost in patients with severe CAP in ICUs was investigated; the necessity of IMV or NIMV, the presence of comorbidity, such as sepsis, COPD, AF, and CHF; low levels of albumin, and mental status disorder were related to an increase in expenses. On the other hand, the choice of fluoroquinolone was related to reduced cost.

While the mortality rate of outpatients is 1%–5%, the ratio in patients who are hospitalized during treatment is 12%; it

Table 3. Evaluation of the relationship between PSI, CURB-65, SOFA, and quick SOFA and costs

	Cost Median (Q.1–Q.3)	p
PSI		
Group I–II (n=16)	1649 (1179–2532)	*0.001
Group III (n=22)	2339 (1576–3289)	
Group IV (n=84)	3249 (2069–5026)	
Group V (n=169)	3964 (2181–7004)	
APACHE II		
<20 points (n=144)	3039 (1625–4541)	
>20 points (n=147)	4129 (2230–6900)	**0.001
Quick SOFA		
<2 points (n=205)	3198 (1980–4916)	
≥2 points (n=86)	4071 (1710–8021)	**0.09
SOFA score		
<3 (n=29)	3069 (1470–4281)	**0.06
≥3 (n=262)	3414 (2061–5952)	
CURB-65		
0 (n=12)	3121 (2275–4393)	
1 (n=65)	2477 (1480–3746)	*0.009
2 (n=73)	3592 (2269–5252)	
≥3 (n=141)	4040 (2138–7472)	

Definitive statistics are expressed as the average±standard deviation and median (Q.1–Q.3)
 *Kruskal–Wallis test was used; **Mann–Whitney U test was used
 Q: quartile; PSI: pneumonia severity index; APACHE: acute physiology and chronic health evaluation; SOFA: sepsis-related organ failure assessment; CURB-65: confusion, urea, respiratory rate, and blood pressure-65

reaches up to 40% in patients who require an intensive care follow-up [3]. An adult ICU is of great importance for the follow-up of patients who show critical levels in vital signs. The ICU costs are of great importance for both hospital expenses and social security institutions [17]. Since 2013, a package per day payment system according to the SSI Health Application Communiqué is being performed in intensive care [18]. Patient care is very costly in these units where advanced life support is provided. It is necessary to consider the ICU cost when choosing which patient to place in these units [19, 20]. In the present study, the costs of patients with severe CAP were evaluated according to their relationship with additional diseases, clinical status, vital signs, applied procedures, the length of stay, antibiotics used, and APACHE II, PSI, CURB-65, SOFA, and quick SOFA scores.

In the cost analysis study conducted by Yarkin et al. [21], the treatment cost was calculated as US\$ 382 per person for hospitalized CAP cases. In another study conducted recently in our country, Kosar et al. [22] reported that in CAP cases with an average of 7 days of hospitalization, the average treatment cost is €556. In our study, the average expense of severe CAP cases hospitalized in ICUs was found as TL 5587 (US\$ 2722). Yarkin et al. [21] analyzed service expenses. The application of antibiotics before hospitalization, leukocyte and creatinine levels, left lung and pleural involvements, the amount of antibiotics used, the application duration of the changed drug, and hospitalization and resolution duration have been stated as the factors that increase cost. In the study by Kaplan et al. [23], the average cost of patients with CAP treated in ICUs has been found as US\$ 14294. Kaplan et al. [23] reported the average length of stay in the ICU as 11 days. In the same study, the cost was calculated as US\$ 7,768 for patients 65–69 years and US\$ 5683 for patients ≥90 years. They have concluded this finding to the more complexity of the disease in younger patients [23].

Table 4. Logistic regression analysis related to factors affecting cost

	Univariate			Multivariate		
	RR	95% Confidence interval	p	RR	95% Confidence interval	p
Age, 50–59 years						
<50 years	19.429	4.976–75.854	<0.001	15.356	2.852–82.669	0.001
60–69 years	6.194	2.419–15.861	0.001	1.992	0.538–7.371	0.30
70–79 years	4.963	1.943–12.680	<0.001	1.678	0.451–6.251	0.44
>80 years	4.260	1.694–10.709	<0.001	1.036	0.272–3.938	0.96
Severe sepsis (present)	1.934	1.156–3.234	0.01	0.516	0.236–1.130	0.10
IMV necessity (present)	6.121	3.680–10.182	<0.001	5.694	2.900–11.179	<0.001
NIMV necessity (present)	2.926	1.768–4.838	<0.001	3.234	1.682–6.218	<0.001
Haloperidol use (present)	3.681	1.937–6.997	<0.001	3.044	1.418–6.533	0.004
Vasopressor use (present)	3.954	2.419–6.462	<0.001	2.254	1.053–4.825	0.036
PHI (Class III)						
Group I–II	4.412	0.462–42.132	0.20	1.410	0.117–17.003	0.79
Group IV	14.302	1.806–113.229	0.01	2.896	0.265–31.624	0.38
Group V	20.704	2.672–160.378	0.00	5.614	0.505–62.354	0.16

RR: predicted relative risk shown with the odds ratio and 95% confidence interval; IMV: invasive mechanical ventilation; NIMV: non-invasive mechanical ventilation; PHI: pneumonia health index

In the study by Akyıl et al. [24], no significant difference in cost was reported between patients under and above 65 years, whereas in a more recent study by Kořar et al. [22], the treatment expenses of patients >64 years were found to be significantly higher than those of patients <65 years. In our study, the expense, which was TL 4281 for 50–59 years, decreased to TL 3121 in patients ≥ 80 years. Increased treatment costs can be explained by the extended treatment duration due to the decreased mortality rates in younger patients.

In patients who are applied IMV, serious complications, such as ventilator-associated pneumonia, upper respiratory track pathologies, respiratory muscle weakness, and barotrauma, may develop [25]. In addition, extended IMV increases patient care expenses significantly. Approximately half of the total IMV time is spent to isolate the patient from ventilation. Keeping IMV duration at minimum is an important aim for health professionals in ICUs, reducing complications and costs [26]. In recent years, the use of NIMV in ICU patients with respiratory failure is exponentially increasing [27]. NIMV has several benefits, such as being a vehicle to isolate from ventilation, the inhibition of acute respiratory failure that may develop after extubation, and the treatment of respiratory failure developing after extubation [28]. NIMV reduces intubation duration, the coughing reflex is not suppressed, and ventilator-associated pneumonia ratios are also decreased [29]. In our study, the applications of IMV and NIMV are shown to be associated with increased cost. In our study, patients who needed IMV stayed at the hospital for a longer time as expected. Similarly, the hospitalization duration of patients to whom NIMV was applied was longer than that of patients without the need of NIMV. Thus, IMV- and NIMV-applied patients' expenses are high due to longer stay at the ICU.

The presence of severe sepsis is seen as an important condition that increases cost since it requires IMV and NIMV and prolongs hospitalization. The presence of specialized physicians in ICUs and the application of infection control programs are reasonable solutions.

The APACHE score system was developed by Knaus et al. [11]. When the APACHE II score is calculated, the worst values within the first 24 h are used. It is a good measuring device to estimate the ICU mortality [30]. In a study where pneumonia scoring systems (CURB-65, SOFA, and PSI) were compared in terms of mortality prediction for 101 patients with severe CAP with the need for mechanical ventilation in the ICU, the APACHE II score (>20 points) was used as an independent determinant of mortality [31].

In our study, when 291 patients with severe CAP were grouped according to the APACHE II scores, expenses were higher in patients with high APACHE II scores (>20 points).

There are many studies that have investigated the values of PSI and CURB-65 scoring systems to evaluate hospitalization in ICUs due to CAP [2]. After the CAP diagnosis, the decision of where to perform the treatment is based on the CURB-65 and PSI indexes. The PSI Group IV and V patients, as well as CURB-65 patients with a score >2, undergo inpatient treatment [32]. Mortality risks are determined by PSI scor-

ing systems, whereas mortality risks are mostly high in PSI Groups IV and V, and hospitalization is advised [33]. In the CURB-65 scoring system, the presence of five parameters, including confusion, uremia, respiration rate, hypotension, and age limit up to 65 years, is examined, and 1 point is given for each criterion. Patients with scores ≥ 3 frequently require inpatient treatment in ICUs [34]. In our study, the CURB-65 score being ≥ 3 increased expenses. This result is an expected outcome due to increased severity. High scores can be an instructive determinant for SGK in the determination of cost.

Today, the daily cost of ICU drugs shows a more rapid increase in price than that of drugs used in services [35]. In our study, the isolated use of fluoroquinolone group antibiotics has been associated with decreased costs. A distinctive increase in expenses associated with the use of haloperidol and vasopressors is an indication of them being among important expense items. In a multicentered, prospective, randomized study by Rittenhouse et al. [36] that included adult patients with CAP, starting the treatment with cefuroxime axetil increases the cost to 34% compared with levofloxacin. The treatment of CAP with fluoroquinolone causes rapid regression of infection when compared to beta-lactam and macrolide antibiotics. In the literature, the length of stay in the hospital for patients taking fluoroquinolone is found to be <1 day [37, 38]. Since hospitalization duration is an important criterion affecting treatment costs, shortening of the duration can decrease such costs. In our study, the expenses of patients treated with fluoroquinolone were significantly reduced, and their hospitalization (n=86) was shorter than that of patients not taking fluoroquinolone, which is in accordance with previous studies [37, 38].

In our study, the hospitalization duration in patients taking haloperidol, which is mostly used for delirium, is found to be approximately two times longer than for patients who are not treated with haloperidol. In our study, it has been shown that the clinical situations requiring haloperidol treatment increase hospitalization duration and expenses.

In our study, the hospitalization duration in patients treated with vasopressors is shorter than that of patients not treated with vasopressors. The present study showed that since patients requiring vasopressor treatment are more severe cases, longer hospitalization results in increased expenses.

The present study has several limitations. The most significant one is its retrospective design. The other limitation is the absence of involvement of specific centers from all geographic regions for the reflection of countrywide results. Results obtained from four big cities cannot be generalized for all countrywide health institutions. The relatively limited patient number and the economic indicators at the time of treatment and the partial change in health politics are other limitations.

In conclusion, the present study showed the estimated health expenses and factors affecting costs of patients with severe CAP treated in ICUs. We have shown that the application of IMV and NIMV which are essential to survive for patients with CAP, severe sepsis state, and the presence of comorbidities, such as COPD, CHF, and AF, are shown to increase the cost. The presence of specific comorbidities in severe CAP

treated in ICUs and the severity of the disease at the time of application are other factors that increase the cost. Since ICU costs will be high during shock in severe sepsis, the need for mechanical ventilation, and the presence of additional diseases, such as COPD, CHF, and AF, we claim that it is a necessity to consider these parameters during SSI package payments.

Ethics Committee Approval: The study was approved by the Akdeniz University Ethical Committee (January 17, 2018; decision no: 48).

Informed Consent: This is a retrospective multicenter cohort study.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept – A.Ç.; Design – A.Ç., A.G.; Supervision – Z.K., B.E.; Resources – Z.K., B.E.; Materials – E.A., Ö.Ç.; Data Collection and/or Processing – A.G., Ö.Ç.; Analysis and/or Interpretation – A.Ç.; Literature Search – Ö.C.; Writing Manuscript – A.G.; Critical Review – A.Ç., A.G.

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