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Title: Factors affecting cost of patients with severe community-acquired pneumonia in intensive care unit

Short title: Cost of severe community-acquired pneumonia

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Abstract

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

Material and Methods: This retrospective cohort study was conducted between January 2013 - December 2016. A total of 291 sequential patients with severe CAP were included in the study. Patients' demographic and clinical data, need for invasive mechanical ventilation (IMV) or non-invasive mechanical ventilation (NIMV), intensive care severity scores including APACHE-II (Acute Physiology And Chronic Health Evaluation), SOFA (Sepsis-related Organ Failure Assessment), Quick SOFA and pneumonia severity index (PSI) and 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. Median length of intensive care unit stay was 7 days. Forty-six percent of patients had chronic obstructive pulmonary disease (COPD), and 42% had hypertension. Mean cost of each hospitalization was found as 2722 $ (5578 TL). The highest cost was found in 50-59 years-aged patient group, lowest cost was found in the <50 years-aged patients. 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. Presence of COPD, atrial fibrillation, congestive heart failure, hypoalbuminemia, mental state deterioration, in-hospital mortality, severe sepsis, septic shock, mechanical ventilation requirement, haloperidol and vasopressor usage were associated with higher cost; while use of florokinolon was associated with lower cost.

Conclusion: The presence of certain comorbidities and high disease severity in patients with severe CAP hospitalized into ICU increase the cost of in-patient treatment. The need for mechanical ventilation during treatment and presence of sepsis / septic shock were other factors that increase the cost.

Keywords: Cost, severe community acquired pneumonia, drug use, intensive care

Introduction

Community-acquired pneumonia (CAP) is a disease that can be treated in government and private health institutions, polyclinics, emergency services, and inpatient facilities with high costs [1]. Severe pneumonia criteria are defined as acute respiratory insufficiency findings (respiration rate >30/min and PaO_2/FiO_2 <250), severe sepsis–septic shock findings (hypotension, meaning systolic blood pressure is <90 mm Hg and diastolic blood pressure is <60 mm Hg, 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 has been defined as 52% [3]. Pneumonia in patients over the age of 65 years accompanied with chronic obstructive pulmonary disease (COPD), malignity, 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 duration of patients with severe CAP in

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need of mechanical ventilation is found to be 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 cost [4]. Choosing the 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 inpatient 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.

It has been reported that the application of antibiotics within 4 h of hospitalization reduces the length of stay in the hospital, whereas a delay of the application of antibiotics for >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 our knowledge, there has been no comprehensive study regarding the expense of patients with severe Turkish CAP monitored in the intensive care unit. The aim of the present study was to investigate the cost and the factors that influence it in patients with severe CAP treated in intensive care units.

Materials and methods

This was a retrospective multicentered cohort study that aims to determine the hospitalization costs and factors that affect the expenses using 291 consecutive patients with severe CAP (Süreyyapaşa Chest Diseaseas Training Research Hospital, Dokuz Eylül University Hospital, Ankara University Hospital, Akdeniz University Hospital) between January 2013 and December 2016. Patients who have been included in the study were composed of cases who had been accepted to the intensive care unit after emergency service and other services. Demographic properties and clinical findings have been obtained after scanning of epicrisis and 4-year medical records of all cases. Age of the patients, gender, length of stay in the intensive care unit, 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) scores, have been recorded. In addition, the total outcome in the intensive care unit (examination fees, treatment service fees, bed fees, and medication and consumable fees included) has been recorded. The expense of each patient in dollar rate has been calculated upon the date on which patients have been placed in intensive care units.

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 above, the presence of possibly new positive symptoms in lung X-ray. In the elderly, it is 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 SGK payments at the time when patients were placed in intensive care units according to SGK Level 3 costs.

Immunosuppressive diseases: Patients with human immunodeficiency virus infection, who used high doses of immunosuppressive drugs for a long time, with cancer, who developed pneumonia 48 h after being placed in the intensive care unit, and 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). The study was performed in accordance with the Declaration of Helsinki.

Statistical analysis

Data were analyzed using the SPSS version 21.0 package program (SPSS Inc., Chicago, IL, USA) for statistical analysis. In the case of normal or non-normal distributions, continuous numerical data were expressed as average±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, Mann–Whitney U test was used in the case of two groups, whereas Kruskal–Wallis test was used in the presence of more than two groups. For comparison between the groups, chi-square test (χ^2) was used in the evaluation of two independent groups. The correlation between PaO_2/FiO_2 values and cost has been evaluated by Spearman's correlation test. A p-value <0.05 was considered statistically significant. In multivariable logistic regression analysis, as dependent variable, cost variables below and above the median value were used and aimed the detection of independent variants that predict the cost being higher than the median (2932.00 TL) calculated in the present study. 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 who were hospitalized in adult intensive care units in a 4-year retrospective period were included in the study. Demographic findings of all patients, clinical features, and total expenses are shown in Table 1. The comparison of patients in terms of treatment expenses are given in Table 2.

In patients with severe CAP between 50 and 59 years old, the cost was found to be significantly high ($p<0.001$). Statistically significant correlations were detected between COPD ($p=0.009$), AF ($p=0.046$), CHF ($p=0.042$), hypoalbuminemia ($p=0.001$), severe sepsis ($p<0.001$), septic shock ($p<0.001$), IMV and NIMV applications ($p<0.001$), applications of haloperidol and vasopressor, and cost. Expenses were significantly low 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 with confusion ($p=0.013$).

When the relationships between 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 PSI risk class, APACHE II score, CURB-65 score, and cost ($p=0.001$, $p=0.001$, and $p=0.009$, respectively). Expenses were higher in patients who were in PSI Group V, who had an APACHE II score >20 points, and who had a CURB-65 score ≥3 points. The correlation between 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

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expenses of intensive care units. The age of the patients being <50 years has been found to be in correlation with low hospitalization expense.

Discussion

In the present study, the hospitalization expenses and factors that affect the cost in patients with severe CAP in the intensive care unit have been 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 have been related to increase in expenses. On the other hand, the choice of fluoroquinolone has been shown to be 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 reaches up to 40% in patients who require intensive care follow-up [39]. Adult intensive care unit is of great importance for the follow-up of patients who have critical levels in vital signs. The intensive care units' costs are of great importance for both hospitals' expenses and social security institutions [17]. Since 2013, package per day payment system according to the SGK 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 intensive care unit cost while choosing which patient to put in these units [19,20]. In the present study, cost of patients with severe CAP were evaluated according to their relationship with additional diseases, clinical status, vital signs, applied procedures, length of stay, antibiotics used, and APACHE II, PSI, CURB-65, SOFA, and quick SOFA scores.

In the cost analysis study performed by Yarkın et al., treatment cost was calculated as US$382 per person for hospitalized CAP cases [21]. In another study performed recently in our country, Koşar et al. reported that in CAP cases with an average of 7 days of hospitalization, the average treatment cost is €556 [22]. In our study, the average expense of severe CAP cases hospitalized in intense care units was found as 5587 TL (US$2722). Yarkın et al. 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 [21]. In the study by Kaplan et al., the average cost of patients with CAP treated in intensive care units has been found as US$14.294. Kaplan et al. reported the average length of stay in the intensive care unit as 11 days [23]. In the same study, the cost was calculated as US$7768 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].

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 Koşar et al., the treatment expenses of patients >64 years were found to be significantly higher than those of patients <65 years [22]. In our study, the expense, which was 4281 TL for 50–59 years, decreased to 3121 TL 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 IMV-applied patients, 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 intensive care units, reducing complications and costs [26]. In recent years, the use of NIMV in intensive care unit patients with respiratory failure is exponentially increasing [27]. NIMV has several benefits, such as being a vehicle to isolate from ventilation, the

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inhibition of acute respiratory failure that may develop after extubation, and the treatment of respiratory failure developing after extubation [28]. NIMV reduces intubation duration, 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 intensive care unit.

The presence of severe sepsis is seen as an important condition that increases cost since it requires IMV and NIMV and increases hospitalization duration. The presence of specialized physicians in intensive care units 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 intensive care unit 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 intensive care unit, 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 in the determination of hospitalization in intensive care units due to CAP [2]. After CAP diagnosis, the

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decision of where to perform the treatment is based on CURB-65 and PSI indexes. PSI Group IV and V patients as well as CURB-65 patients with a score >2 are inpatient treatment [32]. Mortality risks are determined by PSI scoring 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 to 65 years, is examined, and 1 point is given for each criteria. Patients with scores ≥3 frequently require inpatient treatment in intensive care units [34]. In our study, 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 intensive care unit 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. 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. on adult patients with CAP, starting the treatment with cefuroxime axetil increases the cost to 34% compared with levofloxacin [36]. 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 criteria affecting treatment costs, shortening of the duration can decrease cost. In our study, the expense of patients under fluoroquinolone treatment was significantly reduced, and the hospitalization duration of patients taking fluoroquinolone (n=86) was shorter than that of patients not taking fluoroquinolone, and this is in accordance with previous studies [37,38].

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

In our study, the hospitalization duration of patients taking vasopressor treatment 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 expense.

The present study has several limitations. The most significant limitation is its retrospective design. The other limitation is the absence of involvement of specific centers from all geographic regions for the reflection of country-wide results. Results obtained from four big cities cannot be generalized for all country-wide 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 of our study.

In conclusion, the present study showed the estimated health expense and factors affecting costs of patients with severe CAP treated in intensive care units. We have shown that applications of IMV and NIMV in patients with severe CAP observed in intensive care–although essential for survival–, severe sepsis state, and the presence of comorbidities, such as COPD, CHF, and AF, are shown to increase cost. The presence of specific comorbidities in severe CAP treated in intensive care units and the severity of the disease at the time of application are other factors that increase cost. Since intensive care unit 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 SGK package payments.

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Table 1. The clinical properties of 291 patients who were 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)

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Age, year	68.4±16.8
Cost, TL	5578.5052
Cost, $	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.

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

Variables		Cost (TL) Median (Q.1–Q.3)	p-Value
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**

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

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Table 3. The evaluation of the relationship between PSI, CURB-65, SOFA, and Quick SOFA and cost.

	Cost Median (Q.1–Q.3)	p-Value
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)	**0.001
>20 points (n=147)	4129 (2230–6900)	
Quick SOFA		
<2 points (n=205)	3198 (1980–4916)	**0.09
≥2 points (n=86)	4071 (1710–8021)	
SOFA score		
<3 (n=29)	3069 (1470–4281)	**0.06
≥3 (n=262)	3414 (2061–5952)	
CURB-65		
0 (n=12)	3121 (2275–4393)	*0.009
1 (n=65)	2477 (1480–3746)	
2 (n=73)	3592 (2269–5252)	
≥3 (n=141)	4040 (2138–7472)	

Definitive statistics are expressed as 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.

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Table 4. Logistic regression analysis related to factors affecting cost.

	Univariate			Multivariate		
	RR	95% confidence interval	p-Value	RR	95% confidence interval	p-Value
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

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Group V	20.704	2.672–160.378	**0.00**	5.614	0.505–62.354	0.16

RR, predicted relative risk shown with ODDS ratio and 95% confidence interval; IMV, invasive mechanical ventilation; NIMV, non-invasive mechanical ventilation; PHI, Pneumonia Health Index.