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ABOUT COVER

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AIMS AND SCOPE

The primary aim of *World Journal of Clinical Cases* (*WJCC*, *World J Clin Cases*) is to provide scholars and readers from various fields of clinical medicine with a platform to publish high-quality clinical research articles and communicate their research findings online.

WJCC mainly publishes articles reporting research results and findings obtained in the field of clinical medicine and covering a wide range of topics, including case control studies, retrospective cohort studies, retrospective studies, clinical trials studies, observational studies, prospective studies, randomized controlled trials, randomized clinical trials, systematic reviews, meta-analysis, and case reports.

INDEXING/ABSTRACTING

The *WJCC* is now indexed in Science Citation Index Expanded (also known as SciSearch®), Journal Citation Reports/Science Edition, Scopus, PubMed, and PubMed Central. The 2021 Edition of Journal Citation Reports® cites the 2020 impact factor (IF) for *WJCC* as 1.337; IF without journal self cites: 1.301; 5-year IF: 1.742; Journal Citation Indicator: 0.33; Ranking: 119 among 169 journals in medicine, general and internal; and Quartile category: Q3. The *WJCC*'s CiteScore for 2020 is 0.8 and Scopus CiteScore rank 2020: General Medicine is 493/793.

RESPONSIBLE EDITORS FOR THIS ISSUE

ORIGINAL ARTICLE

Retrospective Study

Influence of overweight and obesity on the mortality of hospitalized patients with community-acquired pneumonia

Ning Wang, Bo-Wei Liu, Chun-Ming Ma, Ying Yan, Quan-Wei Su, Fu-Zai Yin

Author contributions: Su QW and Yang Y carried out the studies, participated in collecting data, and drafted the manuscript; Yin FZ and Ma CM performed the statistical analysis and participated in its design; Wang N and Liu BW participated in the acquisition, analysis, or interpretation of data and drafted the manuscript; all authors read and approved the final manuscript.

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Abstract

BACKGROUND
Obesity is associated with a better prognosis in patients with community-acquired pneumonia (the so-called obesity survival paradox), but conflicting results have been found.

AIM
To investigate the relationship between all-cause mortality and body mass index in patients with community-acquired pneumonia.

METHODS
This retrospective study included patients with community-acquired pneumonia hospitalized in the First Hospital of Qinhuangdao from June 2013 to November 2018. The patients were grouped as underweight (< 18.5 kg/m²), normal weight (18.5-23.9 kg/m²), and overweight/obesity (≥ 24 kg/m²). The primary outcome was all-cause hospital mortality.

RESULTS
Among 2327 patients, 297 (12.8%) were underweight, 1013 (43.5%) normal weight, and 1017 (43.7%) overweight/obesity. The all-cause hospital mortality was 4.6% (106/2327). Mortality was lowest in the overweight/obesity group and highest in the underweight group (2.8%, *vs* 5.0%, *vs* 9.1%, *P* < 0.001). All-cause mortality of overweight/obesity patients was lower than normal-weight patients [odds ratio (OR) = 0.535, 95% confidence interval (CI) = 0.334-0.855, *P* = 0.009], while the all-cause mortality of underweight patients was higher than that of normal-weight

patients (OR = 1.886, 95%CI: 1.161-3.066, P = 0.010). Multivariable analysis showed that abnormal neutrophil counts (OR = 2.38, 95%CI: 1.55-3.65, P < 0.001), abnormal albumin levels (OR = 0.20, 95%CI: 0.06-0.72, P = 0.014), high-risk Confusion-Urea-Respiration-Blood pressure-65 score (OR = 2.89, 95%CI: 1.48-5.64, P = 0.002), and intensive care unit admission (OR = 3.11, 95%CI: 1.77-5.49, P < 0.001) were independently associated with mortality.

CONCLUSION
All-cause mortality of normal-weight patients was higher than overweight/ obesity patients, lower than that of underweight patients. Neutrophil counts, albumin levels, Confusion-Urea-Respiration-Blood pressure-65 score, and intensive care unit admission were independently associated with mortality in patients with community-acquired pneumonia.

Key Words: Body mass index; Overweight; Community-acquired pneumonia; Mortality; Prognosis; Obesity

Core Tip: This study found that the all-cause mortality of community-acquired pneumonia in overweight or obese patients was lower than that in normal-weight patients, and the infection index was lower than that in normal-weight patients. The sample size in this study was large, and it breaks the traditional body mass index grouping method. The grouping method in this study is consistent with the traditional grouping method.

INTRODUCTION

Community-acquired pneumonia (CAP) is a lower respiratory tract infection due to one or more pathogens acquired outside of a hospital setting[1]. This contrasts with pneumonia acquired within the hospital setting, including nosocomial pneumonia and ventilator-associated pneumonia[1]. The incidence of CAP ranges from 10.6 to 44.8 cases per 1000 person-years and increases with age[2]. CAP risk factors include age, smoking, chronic comorbidities (such as diabetes mellitus and chronic lung, renal, heart, or liver disease), orodental/periodontal disease, treatment with proton pump inhibitors, prescription opioids, and high alcohol consumption[3-5]. Pathogens that cause CAP include respiratory viruses, *Streptococcus pneumoniae* (*S. pneumoniae*), *Mycoplasma pneumoniae*, *Haemophilus influenzae*, *Moraxella catarrhalis*, *Chlamydophila pneumoniae*, *Legionella* species, *Staphylococcus aureus*, and Gram-negative rods[6,7]. Complications of pneumonia include parapneumonic effusion, empyema, lung abscess, sepsis, and cardiac complications, such as heart failure, cardiac arrhythmias, and acute coronary syndromes[8,9]. Lower respiratory tract infections are among the top 4 causes of death, and the common infectious cause of death, worldwide[10]. The mortality rate is highly variable, ranging from < 1% to > 30%, depending on comorbidities and findings at presentation[11-13].

The prognostic factors for CAP include sex, cognitive symptoms, high urea levels, high respiratory rate, low blood pressure, age ≥ 65 years, comorbidities (cancer, chronic liver disease, heart failure, cerebrovascular disease, and chronic renal disease), and low or higher body temperature[14,15]. Obesity is associated with increased morbidity and mortality, including increased risk of cardiovascular events and increased risk of certain cancers[16-18].

Nevertheless, several studies have shown that the mortality of obese individuals is reduced in various diseases, a phenomenon that is referred to as the "obesity survival

paradox"[19]. Lacroix *et al*[20] found a negative correlation between body mass index (BMI) and pneumonia mortality in an observational study of 2600 middle-aged American men. In a cohort study of 110000 Japanese adults, BMI (≥ 25 kg/m²) had a protective effect on pneumonia mortality [odds ratio (OR) = 0.7, 95% confidence interval (CI): 0.5-0.8][21]. Thus, in some diseases, obesity has emerged as a protective factor that could improve prognosis and reduce mortality[22-24]. Nevertheless, conflicting results are found in the literature[25,26]. In pneumonia caused by severe acute respiratory syndrome coronavirus 2, obesity is associated with worse outcomes [27], but the present study investigated "classical" CAP, not coronavirus disease 2019.

This study aimed to investigate the relationship between BMI and all-cause mortality of CAP and to examine the mechanism of overweight/obesity as a protective factor in CAP prognosis. The results could help our understanding and management of CAP.

MATERIALS AND METHODS

Study design and patients
This study was approved by the Ethics Committee of the First Hospital of Qinhuangdao, and all participants provided written informed consent. This retrospective study included patients with CAP hospitalized in the First Hospital of Qinhuangdao from June 2013 to November 2018.

All patients were diagnosed with CAP according to the clinical guidelines developed by the Respiratory Society of the Chinese Medical Association[28]. The exclusion criteria were: (1) Hospital-acquired pneumonia (HAP; *i.e.*, pneumonia at 48 h after admission); (2) Pulmonary tuberculosis, pulmonary tumors, non-infectious pulmonary interstitial disease, pulmonary edema, atelectasis, pulmonary embolism, pulmonary eosinophilic infiltration, and pulmonary vasculitis caused by other factors, < 18 years of age; or (3) Immunosuppression, which was defined as current, 28-d use of oral prednisolone at any dose, or other immunosuppressive drugs (*e.g.*, methotrexate, azathioprine, cyclosporine, and anti-TNF-α agents), or patients known to have received solid organ transplantation.

Assessment of BMI
All patients had their weight and height measured on admission as part of a nutritional risk assessment score. BMI was calculated as height/weight². Patients were classified into BMI subgroups: (1) Underweight (BMI < 18.5 kg/m²); (2) Normal weight (BMI 18.5-23.9 kg/m²); and (3) Overweight/obesity (BMI ≥ 24 kg/m²)[29].

Patient assessment
Severity assessment scores on admission included the CURB-65 score (*i.e.*, disturbance of consciousness, urea > 7 mmol/L, respiratory rate ≥ 30 breaths/min, systolic blood pressure (SBP) < 90 mmHg and/or diastolic blood pressure (DBP) ≤ 60 mmHg, age ≥ 65 years old)[30]. One point was allocated for each item, five points in total. A score of 0-1 points indicated low risk, 2 points indicate moderate risk, and 3-5 points indicated high risk[30].

Outcome
The primary outcome was all-cause hospital mortality, defined as the ratio of the total number of deaths from all causes during the study period to the total number of people included in the study.

Data collection and definitions
The demographic and clinical characteristics, laboratory biochemical indicators measured for the first time after admission, and other risk factors [including a history of diabetes, use of a ventilator during the disease, and transfer to intensive care unit (ICU)] were collected from the hospital medical record database, and whether the patient terminated hospitalization due to death–an event that was duly recorded. The normal value of white blood cells (WBC) was 3.5-9.5 × 10⁹/L. The normal value of neutrophils (NEUT) was 1.8-6.3 × 10⁹/L. The normal value of C-reactive protein (CRP) was 0-10 mg/L. The normal value of blood urea nitrogen (BUN) was 2.86-8.20 mmol/L. The normal value of albumin (ALB) was 35.0-55.0 g/L. Death of the patient was queried through the medical record system. If the patient's discharge order was death, then the patient was considered an in-hospital death. Death was judged based

on respiratory and cardiac arrest, not including brain death.

Statistical analysis

All data were analyzed using SPSS 21 (IBM, Armonk, NY, United States). Data are expressed as medians (interquartile range) or a numerical value with percentage. When data were not normally distributed, the values were log-transformed for analysis. Categorical variables were analyzed using the chi-square test. Continuous variables were analyzed using Student's *t*-test (two groups) or analysis of variance (ANOVA) with the least significant difference post hoc test (more than two groups). Multiple logistic regression analyses were used to examine the association between the survival state and the observation index. Statistical significance was established at *P* < 0.05.

RESULTS

Characteristics of the patients according to BMI

This study identified 2500 patients with CAP, of which 2327 patients had available BMI data (173 patients were excluded due to a lack of BMI data). There were 297 (12.8%) underweight patients, 1013 (43.5%) with a normal weight, and 1017 (43.7%) overweight/obesity (Table 1). There were statistically significant differences among the three groups in terms of age, sex, diabetes history, consciousness, SBP, DBP, NEUT, CRP, BUN, ALB, use of a ventilator, CURB-65 score, ICU admission, and death (all *P* < 0.05). Mortality was lowest in the overweight/obesity group and highest in the underweight group (overweight/obesity: 2.8%, *vs* normal: 5.0%, *vs* underweight: 9.1%, *P* < 0.001). According to the CURB-65 class, the number of low-risk CAP cases was highest in the overweight/obesity group (overweight/obesity: 73.2%, *vs* normal: 66.6%, *vs* underweight: 52.5%, *P* < 0.001). Accordingly, the proportion of patients admitted to the ICU was lowest in the overweight/obesity group (overweight: 12.1%, *vs* normal: 18.0%, *vs* underweight: 20.5%, *P* < 0.001).

Some infection indicators, such as WBC, NEUT, CRP, and BUN, were higher in the underweight group than in the overweight group. The ALB levels in the underweight group were lower than in the overweight/obesity group [median, 33.0 *vs* 36.9 g/L, *P* < 0.001. The proportion of patients with confusion was higher in the underweight group than in the overweight/obesity group) 16.8% *vs* 6.7%, *P* < 0.001]. The history of diabetes in the overweight/obesity group was higher than in the underweight group (25.7% *vs* 12.6%, *P* < 0.001).

Characteristics of the patients according to survival

Table 2 shows the clinical and laboratory characteristics of the 2327 patients with CAP and according to mortality. The < 65-year-old patients represented 43.0% of the survivors, compared with 57.0% for those > 65 years old (*P* < 0.001). The overweight/obesity group's survival rate was higher than that of the underweight group (44.5% *vs* 12.2%, *P* < 0.001). The patients with a history of diabetes represented 37.9% of the deaths. According to the CURB-65 score, the high-risk group had the lowest survival rate, while the low-risk group had the highest survival rate (*P* < 0.001).

Compared with the non-survival group, the survival group was less likely to spend time in the ICU (14.0% *vs* 52.8%, *P* < 0.001). In addition, the hospital days and the frequency of ventilator use in the non-survival group were higher than in the survival group (both *P* < 0.05). The levels of WBC, NEUT, CRP, and BUN in the death group were higher than in the survival group (all *P* < 0.001). Finally, ALB levels in the survival group were higher than in the mortality group (*P* < 0.001).

Multivariable analysis

Table 3 shows univariable and multivariable logistic regression analyses for in-hospital mortality of 2327 patients with CAP. The univariable analyses showed that diabetes history, WBC, NET, CRP, ALB, CURB-65 risk stratification, BMI, and ICU admission were significantly associated with all-cause mortality (all *P* < 0.05). In the univariable analyses, the all-cause mortality of overweight/obesity patients was lower than that of normal-weight patients (OR = 0.54, 95%CI: 0.33-0.86, *P* = 0.009), while the all-cause mortality of underweight patients was higher than that of normal-weight patients (OR = 1.89, 95%CI: 1.16-3.07, *P* = 0.010). The multivariable analysis showed that abnormal NEUT counts (OR = 2.38, 95%CI: 1.55-3.65, *P* < 0.001), abnormal ALB levels (OR = 0.20, 95%CI: 0.06-0.72, *P* = 0.014), high-risk CURB-65 score (OR = 2.89,

Table 1 Clinical and laboratory characteristics of 2327 patients admitted to hospital with pneumonia in different body mass index groups

Characteristics	BMI categories (kg/m²)			*P* value
	< 18.5 (*n* = 297)	18.5-23.9 (*n* = 1013)	≥ 24 (*n* = 1017)	
Age (yr), (median, IQR), *n* (%)	77 (63, 84)	68 (56, 79)[a]	65 (53, 77)[c]	< 0.001
< 65	80 (26.9)	416 (41.4)[a]	476 (46.8)[b,c]	< 0.001
≥ 65	217 (73.1)	597 (58.9)[a]	541 (53.2)[b,c]	
Sex, *n* (%)				0.025
Male	156 (52.5)	617 (60.9)[a]	581 (57.2)	
Female	141 (47.5)	396 (39.1)[a]	436 (42.8)	
Diabetes history, *n* (%)				0.002
No	260 (87.4)	995 (81.3)	758 (74.3)[b,c]	
Yes	37 (12.6)	185 (18.7)	259 (25.7)[b,c]	
Consciousness, *n* (%)				< 0.001
Conscious	247 (83.2)	919 (90.7)[a]	948 (93.3)[c]	
Confusion	50 (16.8)	94 (9.3)[a]	69 (6.7)[c]	
RR (breaths/min), (median, IQR), *n* (%)	20 (20, 21)	20 (20, 20)[a]	20 (20, 20)	0.036
< 30	282 (94.9)	975 (96.2)	974 (95.8)	0.597
≥ 30	15 (5.1)	38 (3.8)	43 (4.2)	
SBP (mmHg), (median, IQR), *n* (%)	121.5 (110.0, 142.0)	127.0 (113.0, 140.0)[a]	130.0 (120.0, 145.0)[b,c]	< 0.001
≥ 90	280 (94.3)	990 (97.7)[a]	1002 (98.5)[c]	< 0.001
< 90	17 (5.7)	23 (2.3)[a]	15 (1.5)[c]	
DBP (mmHg), (median, IQR), *n* (%)	73.0 (65.0, 81.0)	77.0 (70.0, 84.0)[a]	80.0 (70.0, 88.0)[b,c]	< 0.001
> 60	248 (83.5)	890 (87.9)	933 (91.7)[b,c]	< 0.001
≤ 60	49 (16.5)	123 (12.1)	84 (8.3)[b,c]	
WBC (10⁹/L), (median, IQR), *n* (%)	8.56 (6.03, 12.85)	8.19 (5.84, 11.73)[a]	7.99 (5.86, 11.31)[c]	0.039
Normal	159 (53.5)	554 (54.7)	576 (56.7)	0.519
Abnormal	138 (46.5)	459 (45.3)	441 (43.3)	
NEUT (10⁹/L), (median, IQR), *n* (%)	6.75 (4.28, 10.64)	6.03 (3.78, 9.49)[a]	5.68 (3.75, 8.79)[c]	0.002
Normal	125 (42.1)	478 (47.2)[a]	516 (50.7)[c]	0.025
Abnormal	172 (57.9)	535 (52.8)[a]	501 (49.3)[c]	
CRP (mg/L), (median, IQR), *n* (%)	48.26 (10.55, 105.05)	26.53 (5.96, 79.17)[a]	21.24 (2.92, 72.30)[b,c]	< 0.001
Normal	58 (19.5)	266 (26.3)	313 (30.7)[c]	< 0.001
Abnormal	239 (80.5)	747 (73.7)	704 (69.3)[c]	
BUN (mmol/L), (median, IQR), *n* (%)	6.30 (4.30, 9.45)	5.60 (4.20, 8.10)[a]	5.50 (4.10, 7.38)[c]	0.001
Normal	177 (59.6)	656 (64.8)[a]	721 (71.0)[b,c]	< 0.001
Abnormal	120 (40.4)	357 (35.2)[a]	296 (29.0)[b,c]	
ALB (g/L), (median, IQR), *n* (%)	33.0 (29.9, 37.2)	34.7 (31.0, 38.3)[a]	36.9 (33.2, 40.1)[b,c]	< 0.001
Normal	98 (33.0)	461 (45.5)[a]	621 (61.1)[b,c]	< 0.001
Abnormal	199 (67.0)	552 (54.5)[a]	396 (38.9)[b,c]	
HOD (d), (median, IQR), *n* (%)	10 (7, 15)	10 (7, 14)	10 (7, 14)	0.599
Ventilator use	47 (16.0)	108 (10.7)[a]	95 (9.4)[c]	0.006

ICU admission	61 (20.5)	182 (18.0)	123 (12.1)[b,c]	< 0.001
CURB-65 score, (median, IQR), *n* (%)	1 (1, 2)	1 (0, 2)[a]	1 (0, 2)[b,c]	< 0.001
Low risk	156 (52.5)	675 (66.6)[a]	745 (73.2)[b,c]	< 0.001
Moderate risk	86 (29.0)	236 (23.3)[a]	205 (20.2)[b,c]	
High risk	205 (20.2)	102 (10.1)[a]	67 (6.6)[b,c]	
Death, *n* (%)	27 (9.1)	51 (5.0)[a]	28 (2.8)[b,c]	< 0.001

[a]$P < 0.05$, body mass index (BMI) 18.5-23.9 kg/m^2 group *vs* BMI <18.5 kg/m^2 group.

[b]$P < 0.05$, BMI ≥ 24 kg/m^2 group *vs* BMI 18.5-23.9 kg/m^2 group.

[c]$P < 0.05$, BMI < 18.5 kg/m^2 group *vs* BMI ≥ 24 kg/m^2 group.

Data are expressed as median with interquartile ranges or *n* with percentiles (%). When data were not normally distributed, they were Log-n transformed for analysis. The CURB-65 score is a tool for assessing the severity of patients with community-acquired pneumonia, including new onset confusion; urea > 7 mmol/L; respiratory rate ≥ 30 breaths/min, systolic blood pressure < 90 mmHg and/or diastolic blood pressure ≤ 60 mmHg; and age ≥ 65 years. BMI: Body mass index; IQR: Interquartile range; ALB: Albumin; BUN: Blood urea nitrogen; CRP: C-reactive protein; DBP: Diastolic blood pressure; HOD: Hospital day; ICU: Intensive care unit; NEUT: Neutrophil granulocyte; RR: Respiratory rate; SBP: Systolic blood pressure; WBC: White blood cell.

95%CI: 1.48-5.64, P = 0.002), and ICU admission (OR = 3.11, 95%CI: 1.77-5.49, P < 0.001) were independently associated with mortality in patients with CAP.

DISCUSSION

Although obesity is associated with increased mortality due to multiple causes[16-18], it is associated with a better prognosis in patients with CAP (the so-called obesity survival paradox)[19-24]. However, conflicting results have been found[25,26], especially regarding the categories of patients at risk of higher mortality. Therefore, this study aimed to investigate the relationship between all-cause mortality and BMI in patients with CAP. The results strongly suggested that overweight/obesity patients accounted for the largest proportion of CURB-65 low-risk patients with CAP. The all-cause mortality of overweight/obesity patients was lower than that of normal-weight patients and NEUT counts, ALB levels, CURB-65 score, and ICU admission were independently associated with mortality in patients with CAP.

This study showed that abnormal NEUT counts were independently associated with a poor prognosis of CAP, which is already well-known[31-34]. Hypoalbuminemia is a well-known marker of adverse prognosis in a number of conditions and can be the result of various underlying conditions such as sepsis, cirrhosis, nephrotic syndrome, protein-losing enteropathy, malnutrition, and frailty[35]. Hypoalbuminemia is also associated with a poor prognosis in hospitalized patients[35,36] and in those with CAP [37,38]. The CURB-65 score is a well-known scoring system for the prognosis of pneumonia in the ICU setting[39,40]. It is based on confusion, uremia, respiratory rate, blood pressure, and age, and it can be used to guide management[41]. Finally, of course, ICU admission indicates a severe condition with a higher likelihood of a poor outcome[42-44].

As a general rule, obesity is associated with a higher risk of surgical-site infections, nosocomial infections, periodontitis, skin infections, and acute pancreatitis[45,46]. In overweight patients, there are recognized changes that include hypoxia, oxidative stress, and insulin resistance. Immune cells adapt to an altered tissue microenvironment by adapting their metabolism, eventually leading to an immune response imbalance, chemotaxis damage, and immune cell differentiation[47]. The relationship between obesity and chronic respiratory diseases, including obstructive sleep apnea and obesity hypopnea syndrome, has also been well described[48]. Obese patients show lung function changes, including decreased lung volume, reduced respiratory compliance, reduced gas exchange, impaired respiratory muscle function, and increased airway resistance[49]. Given that these clinical manifestations collectively indicate an increased risk of infection with bacterial and viral pathogens and drive potential changes in lung function, it is logical to theorize that obese patients would be at increased risk for both the development of pneumonia and for much worse clinical outcomes. It can be intuitively assumed that obese patients are more likely to exhibit adverse clinical outcomes and an increased mortality secondary to pneumonia.

Nevertheless, the risk of developing CAP in obese individuals is lower than in the general population[3,46]. BMI and the prognosis of pneumonia have recently emerged

Characteristics	Survival (*n* = 2221)	Death (*n* = 106)	*P* value
Table 2 Clinical and laboratory characteristics of 2327 patients admitted to hospital with pneumonia in different survival state groups			
Age (yr), (median, IQR), *n* (%)	68 (55, 79)	78.5 (70, 85.25)	< 0.001
< 65	955 (43.0)	17 (16.0)	< 0.001
≥ 65	1266 (57.0)	89 (84.0)	
Sex, *n* (%)			0.206
Male	1287 (57.9)	68 (64.2)	
Female	934 (42.1)	38 (35.8)	
BMI (kg/m^2), (median, IQR), *n* (%)	23.44 (20.57, 25.99)	21.10 (18.40, 24.08)	< 0.001
Underweight	270 (12.2)	27 (25.5)	< 0.001
Normal weight	962 (43.3)	51 (48.1)	
Overweight/obesity	988 (44.5)	28 (26.4)	
Diabetes history, *n* (%)	442 (20.2)	39 (37.9)	< 0.001
Smoking history (yr), *n* (%)	409 (18.8)	10 (9.7)	0.020
Consciousness, *n* (%)			< 0.001
Conscious	2038 (91.8)	77 (72.6)	
Confusion	183 (8.2)	29 (27.4)	
RR (breaths/min), (median, IQR), *n* (%)	20 (20, 20)	20 (19, 24)	0.093
< 30	2135 (96.1)	96 (90.6)	0.010
≥ 30	86 (3.9)	10 (9.4)	
SBP (mmHg), (median, IQR), *n* (%)	130.0 (116.0, 144.0)	130.0 (104.5, 150.0)	0.186
≥ 90	2178 (98.1)	94 (88.7)	< 0.001
< 90	43 (1.9)	12 (11.3)	
DBP (mmHg), (median, IQR), *n* (%)	79.0 (70.0, 86.0)	77.5 (62.8, 86.0)	0.078
> 60	1989 (89.6)	82 (77.4)	< 0.001
≤ 60	232 (10.4)	24 (22.6)	
WBC (10^9/L), (median, IQR), *n* (%)	7.99 (5.80, 11.39)	11.65 (8.67, 16.38)	< 0.001
Normal	1258 (56.6)	32 (30.2)	< 0.001
Abnormal	963 (43.4)	74 (69.8)	
NEUT (10^9/L), (median, IQR), *n* (%)	5.86 (3.74, 9.00)	10.02 (6.88, 14.64)	< 0.001
Normal	1099 (49.5)	20 (18.9)	< 0.001
Abnormal	1122 (50.5)	86 (81.1)	< 0.001
CRP (mg/L), (median, IQR), *n* (%)	24.96 (4.52, 78.38)	52.48 (18.27, 139.64)	< 0.001
≤ 10 mg/L	626 (28.2)	11 (10.4)	< 0.001
> 10 mg/L	1595 (71.8)	95 (89.6)	
BUN (mmol/L), (median, IQR), *n* (%)	5.50 (4.10, 7.70)	8.95 (5.65, 14.33)	< 0.001
Normal	1507 (67.9)	48 (45.3)	< 0.001
Abnormal	714 (32.1)	58 (54.7)	
ALB (g/L), (median, IQR), *n* (%)	35.70 (31.90, 39.20)	31.20 (28.00, 34.30)	< 0.001
Normal	1159 (52.2)	22 (20.8)	< 0.001
Abnormal	1062 (47.8)	84 (79.2)	
HOD (days), (median, IQR)	9 (7, 14)	15 (6, 25)	0.014
Ventilator use, *n* (%)	200 (9.1)	50 (47.6)	< 0.001

ICU admission, *n* (%)	310 (14.0)	56 (52.8)	< 0.001
CURB-65 score, (median, IQR), *n* (%)	1 (0, 2)	2 (1, 3)	< 0.001
Low risk	1542 (69.4)	34 (32.1)	< 0.001
Medium risk	491 (22.1)	36 (34.0)	
High risk	188 (8.5)	36 (34.0)	

Data are expressed as medians with interquartile ranges or *n* with percentiles %. When data were not normally distributed, they were Log-n transformed for analysis. The CURB-65 score is a tool for assessing the severity of patients with community-acquired pneumonia, including new onset confusion; urea > 7 mmol/L; respiratory rate ≥ 30 breaths/min, systolic blood pressure < 90 mmHg and/or diastolic blood pressure ≤ 60 mmHg; and age ≥ 65 years. Normal weight: 18.5 kg/m² BMI ≤ 23.9 kg/m²; Overweight: BMI ≥ 24 kg/m²; Underweight: BMI <18.5 kg/m². BMI: Body mass index; IQR: Interquartile range; ALB: Albumin; BUN: Blood urea nitrogen; CRP: C-reactive protein; DBP: Diastolic blood pressure; HOD: Hospital day; ICU: Intensive care unit; NEUT: Neutrophil granulocyte; RR: Respiratory rate; SBP: Systolic blood pressure; WBC: White blood cell.

Table 3 Univariable and multivariable logistic regression analysis for all-cause mortality of 2327 patients with community-acquired pneumonia

Characteristics	Univariable			Multivariable		
	OR	95%CI	*P* value	OR	95%CI	*P* value
Sex (male *vs* female)	1.299	0.865-1.949	0.207			
Diabetes history	1.718	1.205-2.450	0.003	1.423	0.994-2.037	0.054
WBC (abnormal *vs* normal)	3.138	2.233-4.408	< 0.001			
NEUT (abnormal *vs* normal)	3.559	2.573-4.925	< 0.001	2.378	1.549-3.651	< 0.001
CRP (abnormal *vs* normal)	1.321	1.136-1.537	< 0.001			
ALB (abnormal *vs* normal)	0.029	0.011-0.078	< 0.001	0.201	0.056-0.724	0.014
CURB-65 score (moderate risk *vs* low risk)	3.325	2.058-5.372	< 0.001	1.430	0.742-2.753	0.285
(High risk *vs* Low risk)	8.685	5.307-14.212	< 0.001	2.885	1.476-5.641	0.002
BMI (overweight/obesity *vs* normal weight)	0.535	0.334-0.855	0.009			
BMI (underweight *vs* normal weight)	1.886	1.161-3.066	0.010			
ICU admission	6.904	4.629-10.298	< 0.001	3.113	1.765-5.488	< 0.001

The CURB-65 score is a tool for assessing the severity of patients with community-acquired pneumonia, including new onset confusion; urea > 7 mmol/L; respiratory rate ≥ 30 breaths/min, systolic blood pressure < 90 mmHg and/or diastolic blood pressure ≤ 60 mmHg; and age ≥ 65 years. Normal weight: 18.5 kg/m² BMI ≤ 23.9 kg/m²; Overweight: BMI ≥ 24 kg/m²; Underweight: BMI < 18.5 kg/m². WBC: White blood cell; NEUT: Neutrophil granulocyte; CRP: C-reactive protein; ALB: Albumin; BMI: Body mass index; ICU: Intensive care unit; OR: Odds ratio; CI: Confidence interval.

as a subject of increased and intense study[19-26]. The present study confirms that overweight/obesity patients actually have lower all-cause mortality. This is consistent with the fact that the inflammatory indices of overweight/obesity patients were lower than those of underweight patients, and the majority of overweight/obesity patients were at low CURB-65 risk. Similarly, overweight/obesity patients do not have a higher ICU occupancy rate. On the contrary, underweight patients are more likely to be admitted to the ICU.

Previous studies on the relationship between obesity, pneumonia, and mortality have yielded intriguing observations. For example, an early study by Lacroix *et al*[20] showed a negative correlation between BMI and pneumonia-associated mortality in an observational study of 2600 middle-aged American men. In a prospective study of 110 thousand Japanese adults, it was also found that BMI ≥ 25 kg/m² promoted a protective effect in the context of pneumonia-associated mortality[21], and the trend between BMI and CAP mortality showed a significant inverse relationship (*P* < 0.001). Braun *et al*[50] found that in 763 patients, the 64 obese patients (BMI > 30 kg/m²) had a significantly lower 6-year all-cause mortality compared with normal-weight patients (BMI 18.5-25 kg/m²). Other studies also report similar results[22-24], supporting the

present study. Nevertheless, some points still remain to be clarified. Indeed, Kornum *et al*[25] showed that males were at a higher risk of hospitalization than females, which was not observed in the present study. In addition, the relationship between obesity and clinical outcomes appears to be different between children and adults[26], but the present study did not include children.

Some hypotheses can be formulated to try to explain these results. One of the protective factors involved in the better prognosis of CAP in obesity might be an increase in the relative number and frequency of circulating M1 macrophages in overweight patients. Indeed, in an animal model, the content of macrophages in adipose tissue was positively correlated with adipocyte volume and the extent of obesity[51]. Under the regulation of chemokines, inflammatory factors, and free fatty acids in adipose tissue of obese people, IKKS, which is the activator of NF-κB in macrophages, activates the signal pathway *via* phosphorylation of p65, which stimulates a greater number of macrophages to display the M1 sub-type[52]. The increased number of M1 macrophages form a coronal aggregate that expands around the necrotic adipocytes to form similar foam cells, opening lysosomes and autophagic pathways, allowing macrophages to absorb and degrade the ectopic accumulation of lipid[53]. M1 macrophages can also reduce the acute inflammatory response by increasing PPAR-γ activation, autophagy, and lipid oxidation[54]. There is also hyperleptinemia in obese patients, which is involved in innate and acquired immunity and increases the activity of macrophages, chemotaxis of neutrophils, cytotoxicity of natural killer cells, and the production of T and B cells[55]. This activation of all immune cells could promote bacterial clearance. In an animal model reported in 2007, Hsu *et al*[56] found that ob/ob mice had a leptin deficiency. Using wild-type mice as controls, both the ob/ob and wild-type strains were infected with *S. pneumoniae*. It was found that the ob/ob mice had higher mortality and lower lung bacterial clearance rate, which was related to an impaired phagocytic function of the alveolar macrophages, decreased pulmonary neutrophil counts, and a decrease in bioactive proinflammatory cytokines. Exogenous leptin increased the survival rate and lung bacterial clearance rate of ob/ob mice.

A systematic analysis of 13 randomized controlled trials (*n* = 1954) of glucocorticoids for adult CAP showed that glucocorticoids significantly reduced mortality [risks ratio (RR): 0.58, 95%CI: 0.40-0.4] and significantly lowered the early clinical failure rate in adults with severe CAP (RR: 0.32, 95%CI: 0.15-0.7)[57]. Glucocorticoids shorten the clinical cure time, hospital stay, and ICU stay time and reduce the incidence of pneumonia-associated complications. Glucocorticoids play a key role in anti-viral functions, the immune response, and display anti-inflammatory properties and promote other physiological functions, such that the symptoms of pulmonary parenchyma edema can be relieved in the early stages of inflammation. In the recovery period, glucocorticoids can effectively inhibit the proliferation of capillaries, downregulate collagen, inhibit the proliferation of granulation tissue and scar formation in the lung, and avoid pulmonary fibrosis. In addition, glucocorticoids can combine with lipopolysaccharide, which is the main component of Gram-negative bacterial endotoxins, so that it can effectively reduce the damage caused by endotoxins and relieve the corresponding symptoms. At the same time, it can also improve the microcirculation of patients, effectively avoiding platelet aggregation and thus preventing the formation of thromboses. Studies have shown that glucocorticoids in obese people are higher than in the general population[58,59]. The endogen glucocorticoid axis might be another hypothesis for the results observed in the present study.

In the current study, BMI could not be included in the multivariable analysis because it was the variable that was covariant with the largest number of other variables included in the models. Indeed, being underweight is associated with hypoalbuminemia and an inflammatory condition and with a poor prognosis in a variety of conditions[60-62]. Hence, the independent contribution of BMI to CAP mortality could be assessed, as it is an easy-to-determine factor that could be considered in patient management.

This study has limitations. The patients were all from a single hospital. Therefore, when considering the relatively high incidence of CAP, the sample size was relatively small. In addition, it included only hospitalized patients and did not include patients with mild pneumonia and those who returned home with antibiotics. Finally, due to the study's retrospective nature, only all-cause mortality could be examined, and CAP-specific mortality should be investigated in the future. Additional studies are still necessary to examine the prognostic factors of CAP.

CONCLUSION

The inflammatory index and the severity of pneumonia in overweight/obesity patients with CAP were lower than in the normal-weight group, and the all-cause mortality was lower. NEUT counts, ALB levels, CURB-65 score, and ICU admission were independently associated with mortality in patients with CAP.

ARTICLE HIGHLIGHTS

Research background

Obesity is associated with a better prognosis in patients with community-acquired pneumonia (the so-called obesity survival paradox), but conflicting results have been found.

Research motivation

To investigate the relationship between all-cause mortality and body mass index (BMI) in patients with community-acquired pneumonia.

Research objectives

To investigate the relationship between all-cause mortality and BMI in patients with community-acquired pneumonia.

Research methods

This retrospective study included patients with community-acquired pneumonia hospitalized at the First Hospital of Qinhuangdao from June 2013 to November 2018. The patients were grouped as underweight (< 18.5 kg/m^2), normal weight (18.5-23.9 kg/m^2), and overweight/obesity (≥ 24 kg/m^2). The primary outcome was all-cause hospital mortality.

Research results

Among 2327 patients, 297 (12.8%) were underweight, 1013 (43.5%) normal weight, and 1017 (43.7%) overweight/obesity. The all-cause hospital mortality was 4.6% (106/2327). Mortality was lowest in the overweight/obesity group and highest in the underweight group (2.8% *vs* 5.0% *vs* 9.1%, $P < 0.001$). All-cause mortality of overweight/obesity patients was lower than normal-weight patients [odds ratio (OR) = 0.535, 95% confidence interval (CI): 0.334-0.855, $P = 0.009$], while the all-cause mortality of underweight patients was higher than that of normal-weight patients (OR = 1.886, 95%CI: 1.161-3.066, $P = 0.010$). Multivariable analysis showed that abnormal neutrophil counts (OR = 2.38, 95%CI: 1.55-3.65, $P < 0.001$), abnormal albumin levels (OR = 0.20, 95%CI: 0.06-0.72, $P = 0.014$), high-risk Confusion-Urea-Respiration-Blood pressure-65 score (OR = 2.89, 95%CI: 1.48-5.64, $P = 0.002$), and intensive care unit admission (OR = 3.11, 95%CI: 1.77-5.49, $P < 0.001$) were independently associated with mortality.

Research conclusions

All-cause mortality of normal-weight patients was higher than overweight/obesity patients, and lower than that of underweight patients. Neutrophil counts, albumin levels, Confusion-Urea-Respiration-Blood pressure-65 score, and intensive care unit admission were independently associated with mortality in patients with community-acquired pneumonia.

Research perspectives

This study found that the all-cause mortality of community-acquired pneumonia in overweight or obese patients was lower than that in normal-weight patients, and the infection index was lower than that in normal-weight patients. The sample size in this study was large, and it breaks the traditional BMI grouping method. The grouping method of this study is consistent with the traditional grouping method.

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