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Risk factors for complicated community-acquired pneumonia course in patients treated with β-lactam monotherapy

ABSTRACT

Introduction: We aimed to investigate community-acquired pneumonia (CAP) requiring hospitalisation, empirically treated with β-lactam monotherapy, with 30-day mortality and risk factors predicting its complicated course.

Material and methods: A prospective observational study was conducted at the Pulmonology and Allergology Department in a tertiary care university hospital. 253 consecutive patients diagnosed with CAP requiring hospitalisation were enrolled. Hospital admission was based on PSI or CRB-65 scores, severe comorbidities, signs of intoxication, aspiration risk, social risk considerations, ineffective prior antibiotic treatment.

Results: Fourty seven percent of the subjects had complications on admission, 13% developed new CAP complications during inpatient treatment. Overall, 53% of individuals had a complicated CAP course. 30-day mortality rate was 5.9%. The factors predicting a complicated CAP course were as follows: neuromuscular disease, multilobar opacities on chest X-ray (or computed tomography), and clinically unstable condition as evaluated using Halm's criteria.

Conclusions: The mortality rate in CAP patients treated with β-lactam monotherapy is low. Neuromuscular disease, multilobar opacities, and clinically unstable condition as evaluated using Halm's criteria predict a complicated CAP course.

Key words: community-acquired pneumonia, β-lactam monotherapy, mortality, complications

Adv Respir Med. 2021; 89: 359–368

Introduction

Community-acquired pneumonia (CAP) is the deadliest communicable disease and a major cause of morbidity and mortality worldwide [1]. Regardless of the progress in medical science, better health-care access, including specialised units, CAP prevention, pneumonia mortality still accounts for over 30% of all respiratory disease mortality rates [2]. In most cases of CAP, the patients recover completely, however, a part of them develop a complicated disease course which is linked to increased mortality from 11% to 24% [3]. Parapneumonic effusion is the most common pulmonary CAP complication affecting 20–40% of hospitalised patients [4]. Other frequent complications include empyema, lung abscess, acute respiratory failure and sepsis. There is an established link between complicated CAP course and an increased risk of prolonged hospitalisation, and 30-day mortality [5].

Streptococcus pneumoniae is the leading cause of death in severe CAP [6]. Therefore, timely and appropriate antibiotic management is the foundation for CAP treatment. It should be started empirically and guided by regional treatment recommendations and local microbial antibiotic resistance patterns. Based on the 2019 World Health Organization (WHO) Model List of Essential Medicines, amoxicillin is recommended as the first-choice therapy for CAP [7]. Reported *Streptococcus pneumoniae* penicillin resistance is relatively low in several countries, including Lithuania, where the rates are up to 2% in 2015–2018 [8]. Taking CAP aetiology and local antimicrobial resistance patterns as well as the long-term CAP treatment outcomes data into account, the Lithuanian guidelines for adults' pneumonia

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DOI: 10.5603/ARM.a2021.0070 | Received: 17.01.2021 | Copyright © 2021 PTChP | ISSN 2451–4934 | e-ISSN 2543–6031

diagnostics and treatment were published first in 2006 and later updated in 2016. In both versions β-lactam monotherapy is still recommended as the first-choice inpatient CAP treatment [9, 10].

In agreement with the WHO model, several national CAP guidelines outside the USA also list amoxicillin as first-choice antibacterial treatment [11, 12]. In 2019, ATS and IDSA published the updated CAP guidelines [13] where broad-spectrum and combination antibiotic therapy remains to be recommended for CAP inpatient treatment.

The objective of the study is to investigate CAP treated with β-lactam monotherapy, 30-day mortality and risk factors predicting complicated CAP course.

Material and methods

Study design and population

We have conducted a prospective observational study at the Pulmonology and Allergology Department of Vilnius University Hospital Santaros Klinikos in Vilnius, Lithuania from July 2015 until May 2018. 253 consecutive patients diagnosed with CAP requiring hospitalisation were enrolled. We included all adults with clinical symptoms compatible with pneumonia (fever, cough, dyspnoea, chest pain, sputum production) and the presence of new opacities on chest X-ray or computed tomography. Patients with inherited or acquired immunodeficiency or drug-induced neutropenia were not included in the study. Figure 1 depicts the study design.

Data collection, evaluation and outcomes

The data included clinical symptoms, pre-existing conditions, pneumonia complications on admission, clinical stability evaluation using Halm's criteria [14], and initial antibacterial treatment (Table 1).

A chest X-ray or computed tomography was performed on admission and repeated at least once during the course of the treatment to evaluate the resolution or deterioration of pneumonia or pleural effusion. Inflammatory markers (C-reactive protein levels and white blood cell count) were repeatedly tested during the course of treatment. Pneumonia severity was quantified using PSI/PORT (Pneumonia Severity Index) [15] and CRB-65 (confusion, respiratory rate, blood pressure and age ≥ 65 years) [16] scores.

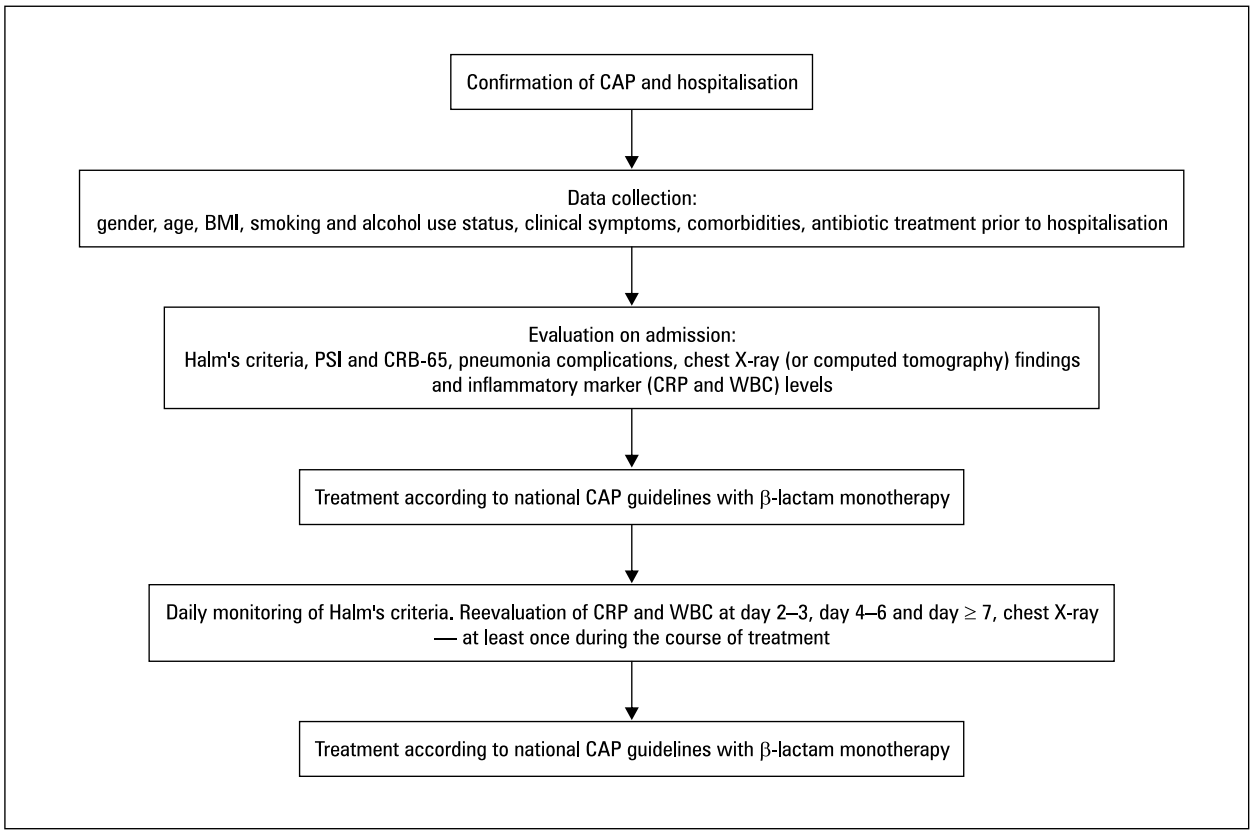

Figure 1. Study design. BMI — body mass index; CAP — community-acquired pneumonia; CRB-65 (confusion, respiratory rate, blood pressure, age ≥ 65 years); CRP — C-reactive protein; PSI — Pneumonia Severity Index; WBC — white blood cell count

Table 1. Baseline characteristics

Characteristics	N = 253
Gender, male	159 (63)
Gender, female	94 (37)
Age, years	57 (± 19)
PSI class	
PSI — I*	47 (19)
PSI — II*	80 (31)
PSI — III	63 (25)
PSI — IV	53 (21)
PSI — V	10 (4)
CRB-65 score	
CRB-65 — 0*	132 (52)
CRB-65 — 1	82 (33)
CRB-65 — 2	36 (14)
CRB-65 — 3	3 (1)
Smoking	144 (57)
Alcohol abuse	25 (10)
Obesity (BMI > 30 kg/m2)	33 (13)
Malnutrition (BMI < 18.5 kg/m2)	13 (5)
Prior antibiotic treatment	91 (36)
Multilobar opacities (on chest X-ray or CT)	95 (37)
Comorbidities	126 (50)
Diabetes mellitus	16 (6)
COPD	27 (11)
Asthma	10 (4)
Bronchiectasis	13 (5)
CHD	76 (30)
Neuromuscular disease	19 (8)
Malignancies	32 (13)
Polymorbidity	50 (20)
Symptoms	
Dyspnoea at rest	98 (39)
Dyspnoea at exertion	153 (61)
Pleuritic chest pain	123 (49)
Cough	193 (76)
Sputum production	108 (43)
Malaise	230 (91)
Confusion	46 (18)
Haemoptysis	36 (14)
Complications on admission	120 (47)
Respiratory failure**	77 (30)
Parapneumonic effusion	49 (19)
Lung abscess	9 (4)
Sepsis	6 (2)
Empyema	5 (2)
Septic shock	3 (1)
Halm's criteria	
Temperature ≤ 37.2°C	121 (48)
Respiratory rate ≤ 24 times/minute	223 (88)
Heart rate ≤ 100 beats/minute	207 (82)
Systolic blood pressure ≥ 90 mm Hg	232 (92)
Arterial oxygen tension ≥ 60 mm Hg or oxygen saturation ≥ 90%	180 (71)
Initial antibacterial treatment	
β-lactam monotherapy	244 (96)
Fluoroquinolone monotherapy***	7 (3)
Antibiotic combinations****	2 (1)

Data are presented as n (%) or mean (SD), unless otherwise stated. *Hospital admission was based on severe comorbidities, advanced age, initial treatment failure. **Confirmed with arterial blood gas test showing PaO_2 of < 60 mm Hg on room air with/without $PaCO_2$ of > 50 mm Hg. Fluoroquinolone monotherapy was used in cases of confirmed or suspected allergic reactions to β-lactams or suspected *Legionella pneumophila* aetiology. Combination therapy with vancomycin was only used in 2 cases where *Staphylococcus aureus* aetiology was suspected.
BMI — body mass index; CAP — community-acquired pneumonia; CHD — coronary heart disease; COPD — chronic obstructive pulmonary disease; CT — computed tomography

All subjects were treated according to the national guidelines for CAP. 96% of patients received β-lactam monotherapy for initial empiric CAP treatment. To investigate the implications for 30-day mortality and factors predicting a complicated CAP course, the group of patients who developed CAP complications over the course of inpatient treatment (n = 32) were compared to individuals who had complication-free course of CAP (n = 118) (Figure 2).

Statistical analysis

We performed the analysis using SPSS software. Categorical variables were expressed as numerical values (percentage) and continuous variables as median (standard deviation (SD)). Data was checked for normality of distribution with the Shapiro-Wilk test. Student's t-test and Mann-Whitney U test were used for comparisons of continuous data. Categorical variables were analysed with the chi-square test. A bivariate analysis was made to identify risk factors significantly associated with CAP complications. Covariates reaching significance from the bivariate analysis were included in the multivariate model. Multivariate logistic regression was performed with CAP complications as the dependent variable and the results reported as odds ratios (ORs) and 95% confidence intervals (95% CIs). A p-value of < 0.05 was considered statistically significant.

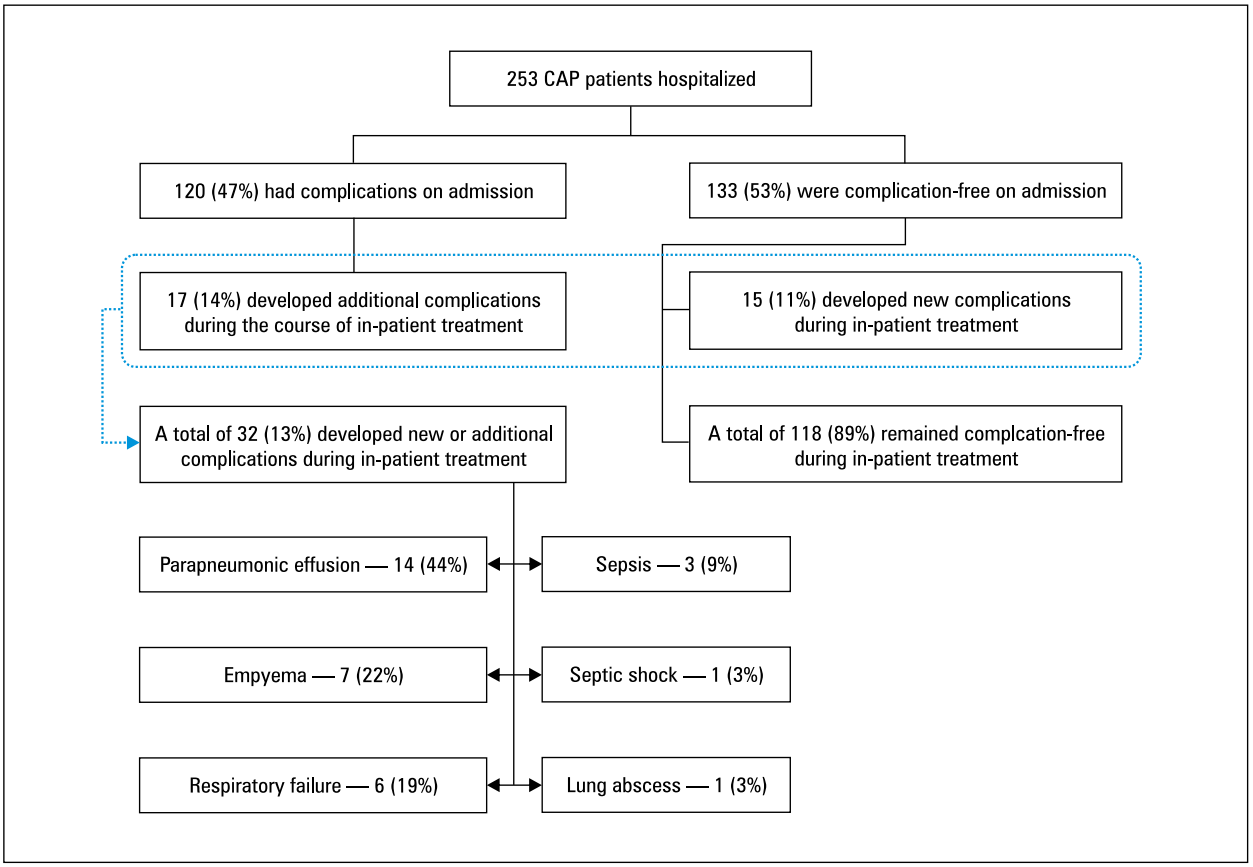

Figure 2. Patient selection for comparison groups and CAP complications developed during the course of inpatient treatment. CAP — community acquired pneumonia

RESULTS

Thirty two (13%) patients developed new CAP complications during inpatient treatment (Figure 2). Over a half of the new complications were parapneumonic effusion or empyema.

Detailed comparison between the patients who developed CAP complications over the course of treatment and those who had complication-free course of CAP is displayed in Table 2.

We found the following clinical symptoms to be significantly associated with complicated CAP course: dyspnoea at rest (50% vs 29%) and exertion (72% vs 52%), and pleuritic chest pain (66% vs 42%). Clinical stability as evaluated using Halm's criteria also proved to be associated with CAP complications. In the complicated CAP group, there was significantly higher percentage of clinically unstable patients than in complication-free CAP group (91% vs 58%).

Radiological evaluation contributes to CAP complications. Only 20% of those with complication-free CAP course had multilobar involvement in contrast with 66% of those with CAP complications. Furthermore, the rate of COPD, neuromuscular diseases, and polymorbidity were all significantly different at 5% level in the comparison groups.

Therefore, we conclude that dyspnoea and pleuritic chest pain, clinically unstable condition as evaluated using Halm's criteria, multilobar opacities and comorbidities are associated with (or contribute to) CAP complication development. However, after multivariate analysis only neuromuscular diseases, multilobar opacities on chest X-ray (or computed tomography) and clinically unstable condition as evaluated using Halm's criteria were identified as independent CAP complication risk factors (Table 3).

Time to radiological resolution was significantly longer for patients who developed CAP complications during in-hospital treatment. The average in-hospital stay was 9 (± 5) days. Patients with CAP complications required longer inpatient treatment (13 [± 8] vs 8 [± 3] days).

There was no significant difference regarding median CRP or WBC levels on admission or at day 2–3 between the patient groups who developed and did not develop CAP complications. However, CRP and WBC values were detected significantly

Table 2. Comparison between the patients who developed community-acquired pneumonia (CAP) complications over the course of treatment and those who had complication-free course of CAP

Characteristics	Complicated CAP course (n = 32)	Complication-free CAP course (n = 118)	P-value
Gender, male	21 (66)	66 (56)	0.420
Gender, female	11 (34)	52 (44)	0.420
Age, years	57 (±18)	55 (±20)	0.619
PSI class IV–V	9 (28)	26 (22)	0.485
CRB-65 score 2–4	4 (13)	14 (12)	1.000
Smoking	18 (56)	60 (51)	0.691
Alcohol abuse	5 (16)	6 (5)	0.057
Obesity	2 (8)	15 (16)	0.518
Malnutrition	2 (8)	6 (7)	0.679
Symptoms			
Dyspnoea at rest	16 (50)	34 (29)	0.034
Dyspnoea at exertion	23 (72)	61 (52)	0.046
Pleuritic chest pain	21 (66)	49 (42)	0.017
Cough	27 (84)	88 (75)	0.346
Sputum production	15 (47)	44 (37)	0.415
Malaise	31 (97)	106 (90)	0.301
Confusion	8 (25)	15 (13)	0.101
Haemoptysis	4 (13)	14 (12)	1.000
Comorbid conditions			
Diabetes mellitus	2 (6)	5 (4)	0.641
Bronchiectasis	4 (13)	5 (4)	0.098
Asthma	3 (9)	3 (3)	0.112
COPD	7 (22)	7 (6)	0.012
CHD	11 (34)	31 (26)	0.381
Malignancies	4 (13)	19 (16)	0.785
Neuromuscular disease	9 (28)	4 (3)	0.000
Polymorbidity	12 (38)	15 (13)	0.003
Unstable as evaluated using Halm's criteria			
Temperature > 37.2°C	20 (63)	65 (55)	0.548
Respiratory rate > 24 times/minute	3 (9)	4 (3)	0.167
Heart rate > 100 beats/minute	3 (9)	15 (13)	0.765
Systolic blood pressure < 90 mm Hg	1 (3)	9 (8)	0.690
Arterial oxygen tension < 60 mm Hg or oxygen saturation < 90%	15 (47)	0 (0)	NA
Clinically stable (as evaluated using all Halm's criteria)	3 (9)	50 (42)	0.000
Multilobar opacities (on chest X-ray or CT)	21 (66)	23 (20)	0.000
Complete radiological resolution	10 (31)	64 (54)	0.028
Time to radiological resolution, days	9 (± 4)	6 (± 3)	0.030
Inpatient stay, days	13 (± 8)	8 (± 3)	0.000
30-day mortality	5 (15.6)	3 (2.5)	0.011

Data are presented as n (%) or mean (SD), unless otherwise stated; CCHD — coronary heart disease; COPD — chronic obstructive pulmonary disease, CT — computed tomography

Table 3. Adjusted odds ratio (OR) and 95% onfidence intervals (CI) for independent predictors of community-acquired pneumonia (CAP) complication risk

Predictors of CAP complication risk	OR	95% CI	P-value
Neuromuscular disease	20.440	3.026–138.083	0.002
Multilobar opacities (on chest X-ray or CT)	7.028	2.068–23.888	0.002
Clinically unstable (as evaluated using Halm's criteria)	5.422	1.082–27.174	0.040

CAP — community-acquired pneumonia; CT — computed tomography

Table 4. C-reactive protein (CRP) and white blood cell (WBC) count levels during the course of treatment in the comparison groups

CRP and WBC levels	Complicated CAP (n = 32)	Complication-free CAP course (n = 118)	P-value
CRP on admission, mg/L	196.1 (± 83.8)	190.4 (± 106.2)	0.785
CRP at day 2–3, mg/L	160.6 (± 100.7)	142.3 (± 90.4)	0.451
CRP at day 4–6, mg/L	128.8 (± 75.3)	71.6 (± 66.9)	0.001
CRP at day ≥ 7, mg/L	90.7 (± 69.8)	38.0 (± 37.0)	0.000
WBC on admission, x 10^9/L	12.0 (± 4.8)	11.6 (± 5.9)	0.725
WBC at day 2–3, x 10^9/L	9.1 (± 2.5)	8.8 (± 4.2)	0.764
WBC at day 4–6, x 10^9/L	9.2 (± 3.1)	8.3 (± 3.1)	0.262
WBC at day ≥ 7, x 10^9/L	9.9 (± 3.4)	7.7 (± 3.1)	0.020

Data are presented as mean (SD); CAP — community-acquired pneumonia; CRP — C-reactive protein; WBC — white blood cell count

higher in patients with CAP complications later during the treatment course (day 4–6, day ≥ 7) (Table 4). ROC curves were constructed to assess the discriminatory power of CRP and WBC levels over the course of treatment in identifying people with CAP complications. The areas under the curve (AUC) for CRP at day 4–6, CRP at day ≥ 7 and WBC at day ≥ 7 were respectively: 0.726; 0.732 and 0.703.

Overall, 30-day mortality rate was 5.9% (n = 15). Patients who developed new CAP complications during in-hospital treatment had 15.6% mortality rate, whereas those who had complication-free course of CAP — 2.5%. CAP complications substantially increased mortality risk (RR = 7.099; 95% CI, 1.598–31.544).

For each patient who died all the medical records were thoroughly reviewed to establish the contributions of CAP to death. High comorbidity burden, poor functional reserve and advanced age were major contributors to mortality in two-thirds of the patients. CAP was judged to be the direct cause of death in one-third (progressing respiratory failure, cardiopulmonary arrest prior to stabilisation of CAP, etc.).

Discussion

The main findings of the study are as follows. First, the mortality rate in CAP patients treated according to national guidelines with β-lactam monotherapy is relatively low. Second, CAP complications significantly increase mortality risk. Third, multilobar radiological involvement, concomitant neuromuscular disorder and altered vital signs as characterised using Halm's criteria were independent risk factors for CAP complications. Below, we discuss our findings regarding CAP complications, specifically, the implications of multilobar involvement and comorbidities, as well as our CAP mortality outcomes with considerations for antibacterial treatment choices.

We have identified multilobar opacities as a significant independent risk factor for CAP complications. There have been studies demonstrating a link between bilateral radiographic CAP infiltrates and unfavourable disease outcomes [17]. The predictive value of multilobar radiographic involvement is well recognised and therefore has been incorporated both into SMART-COP pneumonia scoring system [18]

and the 2007 IDSA/ATS criteria for defining severe CAP [13]. In their systemic review for the prognosis of multilobar pneumonia, Mannu *et al*. have concluded that multilobar radiographic involvement is an independent risk factor for CAP mortality and there also might be an association between multilobar opacities and complicated disease recovery or need for intensive care [19]. Our findings coincide with earlier research — we have demonstrated a sevenfold increase in CAP complication risk in patients with multilobar opacities. While the exact mechanism is unknown, multilobar infiltration is thought to be influenced by both the invasive features of the causative microbe and the host's inflammatory response to the infection. In a study by Cillóniz *et al*., multilobar opacities are regarded as a separate pulmonary CAP complication [20].

An elevated respiratory failure risk in individuals with neuromuscular comorbidities is quite well established — the patients with neuromuscular disorders develop respiratory muscle weakness, which in turn causes hypoventilation, steadily progressing and causing respiratory failure [21]. A study in Hong Kong analysing a group of patients with motor neuron disease revealed pneumonia as the major cause of death in 54.8% and respiratory failure in 40.5% of the subjects [22]. Interestingly, patients with neuromuscular disorders in our study had an elevated risk not only for respiratory failure but also for other CAP complications, mechanisms for which are most likely multifaceted and overlapping.

Our study demonstrated a relatively low 30-day mortality rate (5.9%). Even lower mortality rate was recorded in the complication-free patient group (2.5%). Numerous previous studies have shown varying mortality results ranging from 3.4% to 26.8% [23]. Waterer *et al*. (2018) were investigating CAP in-hospital deaths and have found CAP to be the direct cause of death in about half (51.9%) of their patients [24]. In our study, after conducting a manual case-by-case analysis of each CAP death, we found that only one-third was caused directly by CAP. Whereas, in two-thirds of cases, death was linked to older age, severe comorbidities and frailty. Host factors contribute decisively to outcomes of infectious diseases, and CAP is no exception. The population of older adults is growing by 2% each year [25] and, in part because of ageing population, the prevalence of chronic non-communicable diseases and disability increases. People at the advanced age and with severe or multiple long-term conditions have a higher general vulnerability to acute health threats such as CAP [26]. Higher Charlson Comorbidity Index scores are associated with higher risk of in-hospital mortality and aid in predicting pneumonia outcomes [27].

Risk factors such as age and long-standing severe chronic illnesses have long been associated with increased CAP mortality, and it appears that in some cases, these non-modifiable risk factors determine the course of CAP while antibiotic choice has a minor role in overall disease outcomes, meaning that some of CAP deaths realistically may not be preventable [24]. This might also partly explain the high variability in reported CAP mortality rates [23].

CAP mortality risk has mostly been investigated in clinical studies analysing different antimicrobial treatment regimens. Overall, pneumococcal CAP mortality rates seem to not have changed significantly over the past 20 years. Consequently, the lack of decreased mortality with increasing widespread use of broad-spectrum antibiotic regimens might support the notion that most culture-negative CAP is not caused by drug-resistant pathogens [28]. In their cohort study, Webb *et al*. (2019) have shown that 39.7% of patients received broad-spectrum antibiotics, but drug-resistant pathogens have been recovered in only 3%. Moreover, a broad-spectrum antibiotic use for CAP may be associated with poor clinical outcomes – higher mortality, longer hospital stay, higher cost and increased risk of *Clostridioides difficile* infection [29]. A fairly recent large multi-centre cluster-randomised trial in the Netherlands supports β-lactam monotherapy as an equivalent to β-lactam-macrolide combination or fluoroquinolone monotherapy with regard to 90-day mortality [30]. Given concerns over increasing drug resistance (macrolides) and safety issues (macrolides, fluoroquinolones), there is a need for measured decision choosing CAP treatment. In the 2017 Essential Medicines List (EML), WHO classifies antibiotics into Access, Watch, and Reserve (AWaR) groups, to improve prescribing decisions and guide antibiotic use for common clinical infections [31]. Recognising the need to stop the inappropriate use of antibiotics, the EML Committee recommends an extension of the AWaRe classification and assumes that most respiratory tract infections can be treated with Access antibiotics [7].

The current IDSA/ATS CAP guidelines have been updated in 2019 [13], and in this revision, the recommended antibiotic choices do not differ significantly from those listed in previous versions. CAP guidelines have also been developed

in other countries outside the USA [11, 12, 32, 33]. Most of CAP guidelines can be divided into two groups according to the recommended first-line antibiotics for hospitalised patients: those in line with the IDSA/ATS (macrolide combination with β-lactams) or those in line with the Northern European (β-lactam monotherapy) CAP guidelines [35]. The principal justification for recommending macrolide and β-lactam combination is coverage of atypical pathogens (*Mycoplasma*, *Chlamydophila*, and *Legionella*). However, there is a worrying lack of epidemiological data regarding atypical CAP pathogens and an unsatisfactory standardisation of testing techniques [36]. On the contrary, the β-lactam monotherapy recommendation is generally based on the substantial prevalence of CAP caused by *Streptococcus pneumoniae*, where atypical pathogen coverage is only used for patients with specific risk factors or failure to achieve clinical stability with β-lactam therapy. There is a growing concern that a lot of guidelines developed by scientific societies and professional associations recommending empirical antibiotic use (including IDSA/ATS CAP guidelines) do not routinely consider antimicrobial resistance in their choices [37].

The Lithuanian national guidelines propose initiating the treatment with β-lactam monotherapy for CAP hospitalised patients and using macrolides or fluoroquinolones only in cases of suspected *Legionella pneumophila* aetiology or whenever a patient has contraindications to β-lactams [10]. In our study, in-hospital treatment was started with β-lactams for 96% of patients. Ongoing national as well as local (our hospital's) antibiotic resistance monitoring programmes demonstrate that β-lactam monotherapy remains an effective first-choice therapy option for inpatient CAP treatment in our population. By demonstrating relatively low mortality rates, our study lends additional support for continued use of β-lactam monotherapy.

Universally used CRP and WBC have a well-documented history of usefulness in assessing the diagnosis and clinical course of CAP [38]. However, our study has showed that the predictive value of these biomarkers is limited. Other authors find some advantages adding CRB to Halm's criteria, i.e. improved predicting adverse outcomes, including 30-day mortality, a need for mechanical ventilation or vasopressor support (MV/VS), the development of a complicated pneumonia, and a combined outcome of the above [39]. In meta-analysis by Viasus *et al.*, CRP shows limited use in determining CAP prognosis [40]. We found that CRB and WBC levels on admission or at day 2–3 do not provide additional information for the prediction of a complicated CAP course. However, CRP values measured at day 4 and later were significantly higher in patients with CAP complications. Our findings may suggest that the early antibiotic treatment escalation should not be based exclusively on CRP response because only later measurements have some predictive power for a complicated disease course.

Strengths and limitations

The strengths of the study include its prospective design and 'real-life' management of CAP. We were able to identify factors statistically significantly associated with CAP outcomes. The data on complicated CAP course in an adult population are limited and therefore, our study adds valuable insights into this matter.

Nevertheless, the study has several potential limitations. First, it was conducted in a single centre. Larger multi-centre studies are necessary to define the potential risk factors for CAP complications more accurately. On the other hand, this is the largest specialised pulmonology unit in the region where CAP patients are treated from all over the country, and it likely represents the whole Lithuanian population rather well. Second, there was no control group receiving alternative antibiotic treatment regimen, e.g., macrolide–β-lactam combination. In our study, the vast majority of patients received β-lactam monotherapy because this was a 'real-life' study representing our actual national clinical practice regarding CAP. The third potential limitation of the paper is a lack of information about CAP microbiological aetiology. However, initial CAP treatment is generally empiric, and in our low *Streptococcus pneumoniae* resistance population, β-lactam monotherapy remains first-choice therapy. Whereas invasive diagnostic testing (cultures obtained from bronchial aspirate or bronchoalveolar lavage samples) is only indicated in cases of initial antibiotic treatment failure.

Conclusions

To sum up, the study has demonstrated that in the low *Streptococcus pneumoniae* resistance population, CAP treatment with β-lactam monotherapy results in relatively low mortality rate. The results provide additional evidence that comorbidities, especially neuromuscular diseas-

es, multilobar opacities and clinically unstable condition as evaluated using Halm's criteria have implications for poor CAP outcomes, whereas the predictive value of early CRP and WBC measurements is limited.

Conflict of interest

None declared.

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