Risk Factors of In-Hospital Mortality in Patients Treated for Pneumonia at a Tertiary Care Centre in Switzerland

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Abstract: Background: Little is known about risk factors upon hospital admission that are associated with in-hospital death of patients hospitalized for bacterial pneumonia. Identifying such factors may help to optimize the treatment and lower the mortality of these patients. Objectives: The aim of the study was to characterize baseline characteristics of patients hospitalized for bacterial pneumonia in Switzerland and to identify risk factors associated with all-cause in-hospital mortality. Methods: Routinely collected electronic health record data of patients discharged from a large Swiss tertiary care hospital between August 2009 and 2017 were analysed. Potential risk factors such as patient demographics, physical examination findings, vital signs, laboratory results, and comorbidities were considered within ±24 h of admission. Univariable and multivariable logistic regression models identified risk factors for in-hospital death. The area under the receiver operating characteristic (ROC) curve was used to compare the identified factors to existing pneumonia scoring systems. Results: Out of 1,781 hospital stays with initial and main diagnosis of bacterial pneumonia, 85 patients (4.85%) died (33.9% female, median age 62.3 years [interquartile range, 52–75]). Age, low systolic blood pressure, underweight, a missing value for body mass index, decreased haemoglobin level, raised C-reactive protein, high urea, high lactate dehydrogenase, concomitant pleural effusion, and cancer were independently associated with in-hospital death. The area under the ROC curve was 0.89 for the multivariable model containing the identified predictors. Conclusions: Our data are consistent with previous trials characterizing patients hospitalized for pneumonia. Additionally, we identified new and independent risk factors associated with in-hospital death among patients treated for bacterial pneumonia. Findings need to be further validated in larger multicentre cohorts.

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Keywords
Bacterial pneumonia · In-hospital mortality · Survival · Switzerland

Abstract
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Introduction

Background Information

According to the Global Burden of Diseases Study 2017, lower respiratory tract infections, including bacterial pneumonia, are the leading cause of death from communicable diseases worldwide [1]. Pneumonia scoring systems such as CURB-65 and Pneumonia Severity Index (PSI) help to determine the severity of community-acquired pneumonia (CAP) and to identify low-risk patients who qualify for outpatient care [2, 3]. However, little is known about risk factors upon hospital admission that are associated with in-hospital death of patients hospitalized for bacterial pneumonia. Currently, no scoring system specifically predicting in-hospital death in patients treated for bacterial pneumonia, whether CAP or hospital-acquired pneumonia (HAP), exists. Rigorous management of bacterial pneumonia is essential, as it represents a life-threatening event, and by identifying risk factors, mortality may be decreased [4].

Purpose

The aim of the study is to characterize baseline demographics of patients hospitalized for bacterial pneumonia in Switzerland and to identify risk factors for in-hospital death from any cause (all-cause mortality).

Methods

Study Design and Study Population

The present study is a retrospective observational cohort study of prospectively collected electronic health care data at the University Hospital Zurich (USZ). USZ is a large 850-bed tertiary care academic medical centre located in Zurich, Switzerland. Data of hospitalized patients of at least 18 years of age discharged between August 2009 and 2017 were analysed. Out of all 287,255 hospital admissions (defined as cases), we included all cases admitted with bacterial pneumonia as the initial or main diagnosis, either (i) ICD-10-coded as J13*, J14*, J15*, and J18.1* (International Classification of Diseases, WHO, Geneva, Switzerland; asterisk means zero or more digits) or (ii) ICD-10-coded as J18.8* or J18.9* with a negative PCR test for seasonal respiratory viruses if performed on admission [5]. All other main diagnoses and outpatient cases were excluded. In the case of multiple admissions of 1 patient, all cases were included. The primary endpoint was defined as in-hospital death irrespective of the length of in-hospital stay.

Measurements

Variables included in this report were patient demographics, physical examination findings, vital signs, laboratory results, and comorbidities. Only the first measured values within ±24 h of admission were considered for analyses. Relevant comorbidities according to the literature [2, 6, 7] were defined based on validated algorithms using ICD-10 codes. Chronic heart failure, chronic obstructive pulmonary disease, asthma, hypertension, hypothyroidism, dementia, diabetes mellitus, depression, alcohol misuse, and cancer (irrespective of metastatic status) were defined according to the algorithm by Tonelli et al. [8] for identifying chronic conditions. Renal failure and liver disease were defined according to the coding algorithm by Quan et al. [9] for Elixhauser comorbidities. In addition, B20*, B21*, B22*, B23*, B24*, F02.4*, O98.7*, R75*, U60*, U61*, and Z21* defined HIV. J90* and J91* defined pleural effusion.

Data Sources

Data were ICD-10 coded and extracted from the data warehouse at USZ. Extracted raw data were imported from "comma-separated values" files into a database management system and processed using structured query language statements.

Definitions

Body mass index (BMI) was categorized according to the World Health Organization definition [10] as underweight (BMI <18.5 kg/m^2), normal weight (BMI 20–25 kg/m^2), and overweight (BMI >25 kg/m^2). Laboratory data were categorized according to the USZ laboratory standard values (reference values in online suppl. Table 1; see www.karger.com/doi/10.1159/000508666). Lactate dehydrogenase (LDH) was categorized as normal LDH (≤480 U/L) and high LDH (>480 U/L). Urea was categorized age dependently as normal urea (<60 years ≤7.14 mmol/L, 60–90 years ≤8.21 mmol/L, >90 years ≤11.07 mmol/L) and high urea (<60 years >7.14 mmol/L, 60–90 years >8.21 mmol/L, >90 years >11.07 mmol/L). For survival estimate, haemoglobin level was categorized as low haemoglobin (<11.7 g/dL) and normal haemoglobin (≥11.7 g/dL). For survival analysis using Kaplan-Meier estimates, C-reactive protein (CRP) was categorized according to quartiles into high CRP (4th quartile >18.12 mg/dL) and low CRP (1st quartile <4.2 mg/dL). Continuous variables with >20% missing values were stratified as categorical, including the category "NA" (not applicable) indicating the lack of a value.

Statistical Analysis

Statistical analyses were performed using the software R, version 3.5.1 (R Foundation for Statistical Computing, Vienna, Austria). Depending on normality of distribution, continuous variables were presented as mean ± SD or as median and interquartile range (IQR), and categorical variables as numbers (n) and percentages (%). For significance testing of continuous variables between groups, t tests or Wilcoxon signed-rank tests were used. To compare categorical variables, χ^2 tests or Fisher's exact tests were used.

Univariable and multivariable logistic regression identified associated factors for in-hospital death. The criterion for inclusion in multivariable analysis was a significance level of $p < 0.1$ in the univariable analysis. Stepwise selection of variables was performed to find the best fitting model according to the Akaike information criterion. Only statistically significant predictors ($p < 0.05$) were retained in the final model. Results are presented as odds ratios (OR) with CI from 2.5 to 97.5%. The area under the receiver operating characteristic (ROC) curve (AUC) was calculated to assess the prognostic value of the selected predictors.

For subgroup analysis, all cases were categorized based on the length of stay of ≤7 and >7 days (cut-off at median length of stay of patients who died in hospital). Multivariable logistic regression

Table 1. Baseline characteristics of study cohort

Variables	All patients (n = 1,781)	NA, %	Survivors (n = 1,696; 95.2%)	Non-survivors (n = 85; 4.8%)	p value
Age, years	65 (52–75)	–	65 (52–75)	73 (66–81)	<0.001
Sex, female	604 (33.9)	–	583 (34.4)	21 (24.7)	0.085
Civil status					0.173
Married/partnered	952 (53.5)	–	899 (53.0)	53 (62.4)	
Single	374 (21.0)	–	364 (21.5)	10 (11.8)	
Widowed/divorced/separated	409 (23.0)	–	389 (22.9)	20 (23.5)	
Other/unknown	46 (2.6)	–	44 (2.6)	2 (2.4)	
Physical examination findings					
BMI, kg/m^2	25.22±8.11	826 (46.4)	25.28±8.19	23.22±4.89	0.163
Systolic BP, mm Hg	126.63±22.03	224 (12.6)	126.96±21.95	119.90±22.80	0.008
Diastolic BP, mm Hg	72.56±13.91	226 (12.7)	72.71±13.79	69.38±15.91	0.047
Body temperature, ° C	37.55±0.95	228 (12.8)	37.56±0.95	37.27±0.78	0.011
Laboratory findings					
Haematocrit, %	36.0 (31.7–40.0)	13 (0.7)	36.10 (31.9–40.0)	31.0 (27.8–36.1)	<0.001
Haemoglobin level, g/dL	12.0 (10.4–13.4)	13 (0.7)	12.00 (10.5–13.4)	10.2 (8.9–11.9)	<0.001
White blood cell count, ×10^9/L	10.6 (7.4–14.6)	13 (0.7)	10.60 (7.4–14.5)	10.1 (7.3–15.7)	0.693
Neutrophil cell count, ×10^9/L	8.3 (5.5–12.1)	52 (2.9)	8.30 (5.5–12.1)	7.5 (5.0–12.7)	0.749
Lymphocyte count, ×10^9/L	0.9 (0.6–1.4)	125 (7.0)	0.90 (0.6–1.4)	0.8 (0.4–1.0)	<0.001
Platelet count, ×10^9/L	228 (167–314)	13 (0.7)	228 (169–314)	233(137–345)	0.882
CRP, mg/dL	10.2 (4.2–18.1)	21 (1.2)	10.0 (4.1–17.9)	14.2 (7.0–24.6)	0.002
Creatinine level, μmol/L	89.0 (70.0–128.0)	61 (3.4)	89.0 (70.0–126.0)	100.5 (72.5–147.8)	0.088
Blood urea level, mmol/L	6.9 (4.6–10.7)	495 (27.8)	6.7 (4.6–10.3)	10.5 (6.7–15.2)	<0.001
Blood glucose level, mmol/L	6.6 (5.6–8.1)	788 (44.2)	6.5 (5.6–8.1)	6.6 (5.9–8.5)	0.564
LDH, U/L	443 (359–565)	952 (53.5)	438 (356–552)	614 (465–907)	<0.001
Sodium, mmol/L	136 (133–139)	45 (2.5)	136 (133–139)	135 (133–140)	0.535
Serum total protein, g/L	66.0 (61.0–71.0)	1,454 (81.6)	66.0 (61.0–71.25)	60.0 (54.5–70.5)	0.075
Albumin, g/L	35.0 (31.0–38.0)	1,019 (57.2)	35.0 (31.0–38.0)	30.0 (25.0–34.5)	<0.001
AST, U/L	29.0 (22.0–41.0)	506 (28.4)	28.0 (22.0–40.0)	33.5 (25.3–57.0)	0.002
ALT, U/L	21.0 (15.0–36.0)	196 (11.0)	21.0 (15.0–36.0)	23.5 (13.0–39.3)	0.961
Comorbidities					
Chronic heart failure	222 (12.5)	–	205 (12.1)	17 (20.0)	0.047
Hypertension	718 (40.3)	–	684 (40.3)	34 (40.0)	1
COPD	309 (17.3)	–	294 (17.3)	15 (17.6)	1
Asthma	51 (2.9)	–	50 (2.9)	1 (1.2)	0.534
Cancer	309 (17.3)	–	273 (16.1)	36 (42.4)	<0.001
Renal failure	502 (28.2)	–	471 (27.8)	31 (36.5)	0.106
Liver disease	80 (4.5)	–	76 (4.5)	4 (4.7)	1
Diabetes mellitus	329 (18.5)	–	314 (18.5)	15 (17.6)	0.954
Hypothyroidism	128 (7.2)	–	125 (7.4)	3 (3.5)	0.262
Dementia	59 (3.3)	–	52 (3.1)	7 (8.2)	0.022
Depression	123 (6.9)	–	117 (6.9)	6 (7.1)	1
Alcohol misuse	48 (2.7)	–	46 (2.7)	2 (2.4)	1
HIV	73 (4.1)	–	73 (4.3)	0 (0.0)	0.094
Pleural effusion	176 (9.9)	–	155 (9.1)	21 (24.7)	<0.001
Comorbidities, n	1.77±1.39	–	1.75±1.37	2.33±1.62	<0.001
Previous admissions, n					
Within the last 2 years	1.76±2.36	–	1.74±2.36	2.11±2.29	0.199
Within the last year	1.08±1.57	–	1.06±1.56	1.54±1.76	0.009
Within the last 6 months	0.67±1.08	–	0.65±1.07	1.01±1.20	0.003
Within the last 90 days	0.40±0.75	–	0.39±0.74	0.65±0.90	0.001
Within the last 30 days	0.17±0.43	–	0.16±0.42	0.36±0.53	<0.001
Length of stay, days	8 (5–12)	–	8 (5–12)	7 (3–13)	0.219

Continuous data are expressed as mean ± SD or median (IQR) where appropriate. Categorical data are expressed as n (%). Laboratory reference values are displayed in Supplement Table 1. NA, not available; BMI, body mass index; BP, blood pressure; CRP, C-reactive protein; LDH, lactate dehydrogenase; AST, aspartate aminotransferase; ALT, alanine aminotransferase; COPD, chronic obstructive pulmonary disease; HIV, human immunodeficiency virus.

Table 2. Multivariable logistic regression analysis

Variables	Univariable analysis			Multivariable analysis		
	OR	95% CI	*p* value	OR	95% CI	*p* value
Age, years	1.04	1.03–1.06	<0.001	1.07	1.04–1.10	<0.001
Systolic BP	0.98	0.97–1.00	0.008	0.98	0.96–0.99	0.009
Normal weight	Ref.			Ref.		
Underweight	3.51	1.36–8.50	0.006	6.08	1.84–19.68	0.003
NA BMI	2.21	1.25–4.17	0.010	2.96	1.39–6.90	0.007
Haemoglobin level	0.77	0.69–0.85	<0.001	0.83	0.71–0.95	0.009
CRP	1.03	1.01–1.05	<0.001	1.04	1.01–1.07	0.002
Normal LDH	Ref.			Ref.		
High LDH	4.42	2.44–8.41	<0.001	5.12	2.26–12.61	<0.001
Normal urea	Ref.			Ref.		
High urea	3.22	1.95–5.47	<0.001	2.11	1.08–4.24	0.031
Cancer	3.83	2.43–5.99	<0.001	3.22	1.73–5.99	<0.001
Pleural effusion	3.26	1.90–5.40	<0.001	3.35	1.63–6.65	<0.001

Definitions: high LDH (>480 U/L), high urea (<60 years >7.14 mmol/L, 60–90 years >8.21 mmol/L, >90 years >11.07 mmol/L). OR, odds ratio; CI, confidence interval; BP, blood pressure; BMI, body mass index; Ref., reference; NA, missing values for each specific variable; CRP, C-reactive protein; LDH, lactate dehydrogenase.

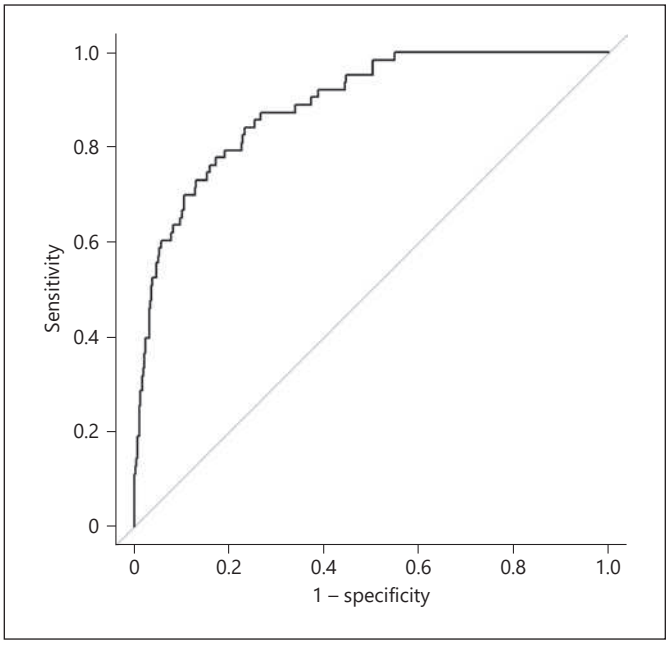

Fig. 1. ROC curve for in-hospital death for the identified risk factors in Table 2.

of the previously identified factors associated with in-hospital death was performed on both subgroups. Additionally, Kaplan-Meier estimate was calculated for overall survival based on the length of in-hospital stay. The log-rank test was used to compare Kaplan-Meier estimates. Significance was accepted for $p < 0.05$.

Results

Study Cohort and Baseline Characteristics

We identified 1,781 cases admitted for bacterial pneumonia. Overall median age was 65 years (IQR 52–75) and 604 (33.9%) were female. The overall median length of stay until either in-hospital death or discharge from hospital was 8 days (IQR 5–12). Table 1 summarizes baseline characteristics of the study cohort stratified by survival (survivors, 95.2%) and in-hospital death (non-survivors, 4.8%). Compared to survivors, non-survivors were significantly older, had a lower systolic and diastolic blood pressure, a lower haematocrit and haemoglobin level, a lower lymphocyte count, and a lower albumin level. In contrast, non-survivors had a significantly higher CRP level, a higher LDH level, a higher blood urea level, and a higher AST level. Chronic heart failure, cancer, dementia, and pleural effusion were more common in non-survivors. Non-survivors also had significantly more comorbidities and were more often hospitalized in the previous year.

Risk Factors of In-Hospital Mortality

For prediction of in-hospital mortality, 43 variables were analysed. Of these, 25 variables with a *p* value <0.1 in univariable analysis qualified for multivariable analysis. In a stepwise multivariable logistic regression analysis, we identified 10 independent factors associated with all-cause in-hospital death of patients hospitalized for the

Table 3. Multivariable logistic regression analysis based on length of stay

Variables	≤7 days (n = 862 cases, n = 47 deaths)			>7 days (n = 919 cases, n = 38 deaths)		
	OR	95% CI	p value	OR	95% CI	p value
Age, years	1.06	1.03–1.10	<0.001	1.06	1.02–1.10	<0.004
Systolic BP	0.98	0.95–1.00	<0.087	0.97	0.94–1.00	<0.023
Diastolic BP	1.00	0.96–1.04	<0.902	1.06	1.02–1.11	<0.007
Norm. weight	Ref.			Ref.		
Underweight	3.79	0.69–18.97	<0.109	6.70	1.18–36.07	<0.026
NA BMI	1.99	0.76–5.81	<0.179	2.60	0.90–8.91	<0.097
Haemoglobin level	0.77	0.63–0.94	<0.011	0.80	0.63–1.00	<0.052
CRP	1.05	1.01–1.08	<0.009	1.03	0.99–1.06	<0.176
Norm LDH	Ref.			Ref.		
High LDH	4.32	1.49–14.12	<0.010	4.48	1.31–18.44	<0.023
Norm urea	Ref.			Ref.		
High urea	3.03	1.26–7.68	<0.015	1.41	0.54–3.77	<0.485
Cancer	2.25	0.93–5.40	<0.069	5.78	2.47–14.00	<0.001
Pleural effusion	3.77	0.92–13.17	<0.047	5.27	2.20–12.59	<0.001

Definitions: high LDH (>480 U/L), high urea (<60 years >7.14 mmol/L, 60–90 years >8.21 mmol/L, >90 years >11.07 mmol/L). OR, odds ratio; CI, confidence interval; BP, blood pressure; BMI, body mass index; NA, missing values for each specific variable; CRP, C-reactive protein; LDH, lactate dehydrogenase.

treatment of bacterial pneumonia (Table 2). Factors were age, low systolic blood pressure, underweight, a missing value for BMI (NA BMI), decreased haemoglobin level, raised CRP level, high urea, high LDH, concomitant pleural effusion, and cancer. For the identified risk factors above, the AUC of the multivariable logistic regression model was 0.89 (Fig. 1).

Prognostic Factors of In-Hospital Death Stratified by Length of Stay

Patients who stayed >7 days were significantly older (68 vs. 63 years, $p < 0.001$), had an increased LDH level (450 vs. 435.5 U/L, $p = 0.014$) and suffered more often of concomitant pleural effusion (14.7 vs. 4.8%, $p < 0.001$) than patients who stayed ≤7 days in hospital. Additionally, the former had multiple comorbidities (2.16 vs. 1.36, $p < 0.001$). However, there was no significant difference in the prevalence of cancer (17.8 vs. 16.8%, $p = 0.612$) in both subgroups. Table 3 compares in a multivariable subgroup analysis all cases with a length of stay ≤7 days (n = 862) to those with a length of stay >7 days (n = 919). Age, decreased haemoglobin level, raised CRP level, high LDH, high urea, and a concomitant pleural effusion are significantly associated with in-hospital death within the first 7 days. Of these factors, age, high LDH, and concomitant pleural effusion were still associated with death after 7 days. Additionally, systolic and diastolic blood pressure, underweight, and cancer are significantly associated with death after 7 days of in-hospital stay.

Estimates of Survival

Figure 2 shows the Kaplan-Meier survival curve of 4 stratified and previously identified factors associated with in-hospital death for 21 days: underweight, high LDH, low haemoglobin, and high CRP. p values were statistically significant in log-rank test comparing each variable ($p < 0.05$).

Discussion

Principal Findings

Of the factors identified, age, systolic blood pressure, blood urea level, cancer, and concomitant pleural effusion are included in either the PSI score [3] or the CURB-65 score [2]. In addition, we found increased CRP level, decreased haemoglobin level, high LDH level, and underweight or a missing value for BMI to be significantly associated with in-hospital death. In Figure 2, we highlighted again the identified risk factors for in-hospital death in 4 Kaplan-Meier survival curves of variables not present in the CURB-65 or PSI score.

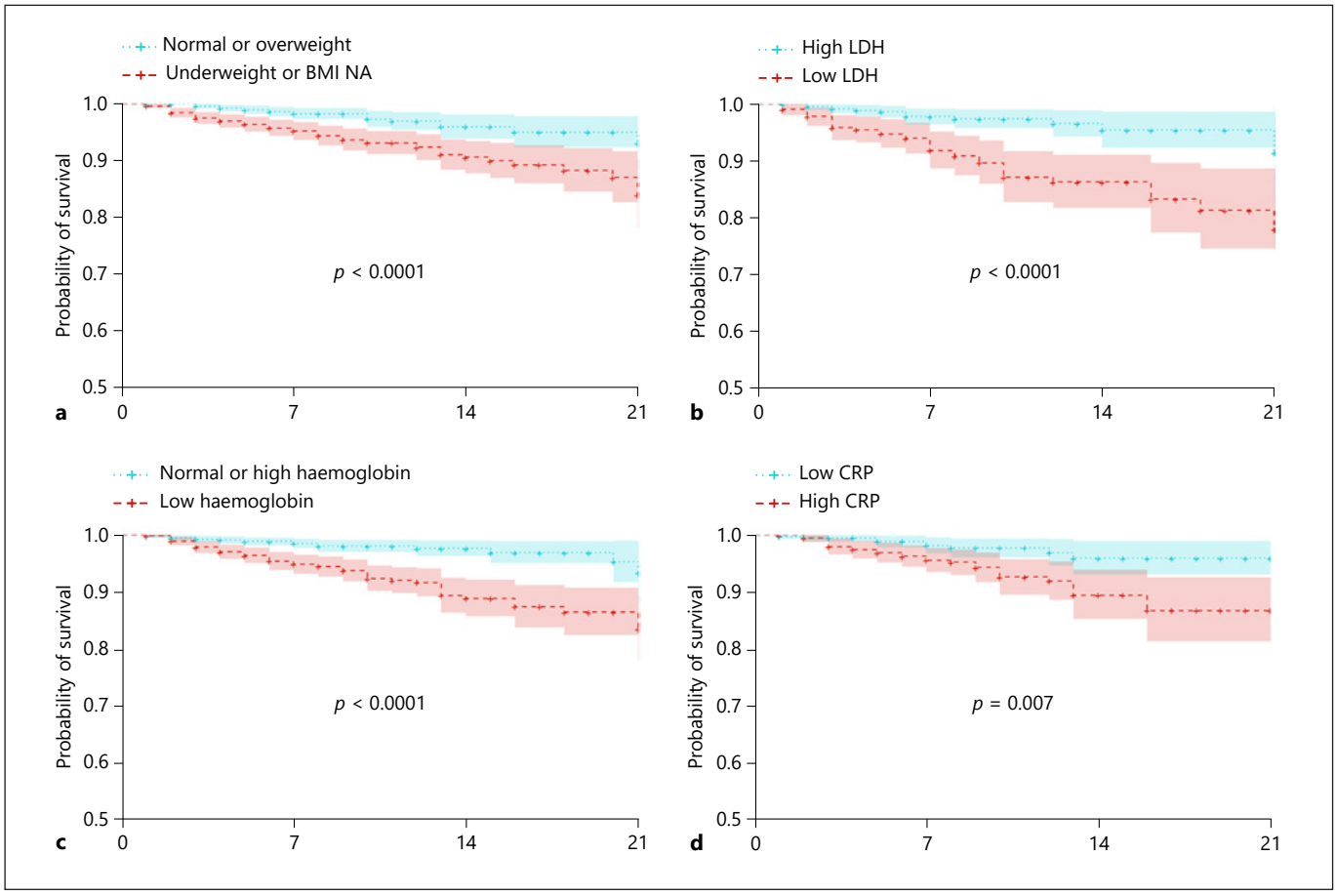

Fig. 2. Kaplan-Meier survival curve of 4 stratified and previously identified factors associated with in-hospital death for 21 days. **a** Comparison of underweight patients (BMI <18.5 kg/m^2) and patients with missing BMI values (BMI NA) vs. obese, normal, and overweight patients (BMI ≥20 kg/m^2). NA, not applicable. **b** Comparison of patients with initial high LDH (>480 U/L) vs. patients with initial normal LDH (≤480 U/L). **c** Comparison of patients with initial low haemoglobin (<11.7 g/dL) vs. patients with initial normal haemoglobin (≥11.7 g/dL). **d** Comparison of patients with initial high CRP (>18.12 mg/dL) vs. patients with initial low CRP (<4.2 mg/dL).

Lee et al. [7] previously described the role of a raised CRP as an independent predictor of 28-day mortality. However, their cut-off defining high CRP was set at 14.3 mg/dL and if added to the CURB-65 score, no additional effect was observed.

The association of anaemia with excess mortality in patients treated for various diseases including pneumonia was previously outlined [11–14]. This finding has been considered by the PSI score through the variable haematocrit, but not by haemoglobin level, which was, in our study, significantly associated with in-hospital death if decreased.

High LDH has been described as a predictor of mortality in patients with AIDS and *Pneumocystis carinii* pneumonia, but not in bacterial pneumonia [15]. Initial high LDH level might be the consequence of chronic heart failure, liver damage, cancer, or sepsis and is a well-known unspecific marker for tissue damage [16]. In-hospital death is possibly associated with the underlying cause that leads to increased LDH, but not due to LDH itself. Nevertheless, liver diseases and markers of liver injuries such as AST, ALT, and albumin did not turn out to be significantly associated with in-hospital death in multivariable analysis. Multivariable regression showed an independent association of cancer and of high LDH with in-hospital death.

Our fourth novel risk factor for in-hospital mortality is weight; either as missing BMI value (NA BMI) or un-

derweight. NA BMI can be explained by severity of disease and consecutive immobilization and, therefore, omission of measuring the weight on a scale. Underweight, on the other hand, is potentially related to malnutrition and cachexia, or other health issues such as hypalbuminaemia which was previously identified as a predictor for mortality in CAP [17]. However, the association of low albumin and mortality was not statistically significant in our study cohort.

In subgroup analysis, we found a different set of prognostic factors based on the length of in-hospital stay of ≤7 and >7 days (Table 3). At initial presentation, haemoglobin level, CRP, and urea only seem to have a prognostic value within the first 7 days of in-hospital stay. After 7 days, we found underweight and cancer to be independently associated with in-hospital death. These factors might be associated with in-hospital death irrespective of pneumonia [18, 19]. On the other hand, cancer has previously been found to be a predictor of poor prognosis in CAP [20].

Comparison to Previous Studies

All-cause mortality in our study (4.8%) was lower compared to similar relevant studies in Europe (9.1%), USA/Canada (7.3%), Latin America (13.3%), and South Korea (9.3%) [17, 21]. However, the prevalence of most comorbidities was lower, which might explain the difference. On the other hand, in a study validating the PSI score, in-hospital mortality was lower despite having similar baseline characteristics [6]. A recent study comparing mortality rates of pneumonia in the European Union between 2001 and 2014 showed higher mortality rates in most countries than in Switzerland. The authors also did not distinguish between CAP and HAP using a similar approach based on ICD-10 codes [22]. The overall median length of stay was 8 days, and the median length of stay of patients who died in-hospital was 7 days ($p = 0.219$; Table 1). These findings seem to be congruent with related studies on pneumonia [23, 24]. Based on this, we defined the cut-off in subgroup analysis (Table 3). With an AUC of 0.89, our identified risk factors seem to have a higher discriminatory power in predicting mortality than existing pneumonia scoring systems. In another study, AUC for predicting mortality was 0.81 for PSI, 0.73 for CURB, and 0.76 for CURB-65 score [25]. However, direct comparison is not possible, mainly due to heterogeneous cohorts and the fact that CURB-65 and PSI score included ambulatory patients. Finally, variables included in the CURB-65 score such as respiratory rate or confusion are missing in our study.

Strengths

Data were routinely collected and extracted from electronic health records and therefore we did not have influence on the variables collected.

The identified factors are relevant for daily clinical practice and may help identifying patients at risk of in-hospital death. Physicians especially need to consider relevant comorbidities such as cancer and concomitant pleural effusion [26]. The studied period of 8 years is the longest compared to pneumonia-related studies in Switzerland and Europe. In contrast to other studies, we did not exclude patients due to other conditions such as previous admissions or a certain comorbidity [2, 3, 7]. Therefore, the study reflects the real-life scenario with an examination of a broad range of clinically relevant variables in a large cohort compared to related studies. Results are likely to be transferable to other hospital settings in Europe.

Limitations

All data come from a single tertiary care hospital and thus potential selection bias and referral bias cannot be excluded. Sample size varies among different variables depending on the individual health care provider ordering specific tests on admission. This concerns particularly physical examination findings and laboratory values. However, patient demographics, comorbidities and, importantly, recordings of in-hospital death were complete. CRP was classified as a categorical variable for survival analysis by Kaplan-Meier estimate. Since a dichotomous classification using the clinical validated cut-off of 5 mg/L would have resulted in too much simplification, we chose to use categorization according to quartiles.

Since microbiology results were not available in the current study, our approach to identify patients with bacterial pneumonia was based on ICD-10 codes. However, ICD-10 codes were added to the diagnoses after patient discharge, and no information was available on whether pneumonia was present on admission or occurred later in the stay. Consequently, we could not distinguish between CAP and HAP, but included all cases coded as bacterial pneumonia and excluded those with positive PCR for respiratory viruses. Therefore, in cases with HAP a prediction of in-hospital mortality based on variables at initial presentation is not possible. However, according to a recent study in Switzerland, the estimated incidence of HAP is up to 15 times lower than the incidence of CAP, making the proportion of potential cases with HAP in our study population considerably small [27]. Ultimately, a validation cohort study with prospective inclusion of CAP is needed.

The identified predictors of mortality cannot be applied to outpatients due to exclusion. In addition, not all variables found in existing pneumonia scores were present. Validation of CURB-65 or PSI score was therefore not possible. Our results have not been validated yet in other cohorts. More data are required, preferably from multiple hospitals, to validate our findings.

Conclusion

This study identified 10 independent risk factors of in-hospital mortality in patients treated for bacterial pneumonia. Of these, raised CRP level, decreased haemoglobin level, high LDH level, and underweight or a missing value for BMI are currently not represented in other pneumonia scoring systems. These results are compatible with large multicentre trials and add additional value and insight into the efforts of reducing mortality of hospitalized patients treated for bacterial pneumonia. However, findings need to be validated in larger multicentre cohorts.

Statement of Ethics

Ethical approval for this study was waived by the local Cantonal Ethics Committee because of the anonymized nature of the data (Waiver No. 2017-00882). Our study adhered to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines [28].

Conflict of Interest Statement

The authors have no conflict of interest to declare.

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Author Contributions

All authors listed above have made substantial contributions in designing the study, acquiring/analysing/interpreting of data, or in drafting/reviewing the manuscript. All authors agree to be accountable for all aspects of the work.

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