3-day mortality in hospitalised community-acquired pneumonia: frequency and risk factors

To the Editor:

Mortality of hospitalised patients with community-acquired pneumonia (CAP) continues to be high and efforts have been made to characterise a subgroup of patients with an emergency presentation defined by a high risk of early clinical deterioration or death in order to target initial management interventions to patients with a high potential of prognosis improvement [1–3]. However, the actual magnitude of an emergency presentation in CAP remains unclear as the most severely affected patients are frequently underrepresented in prospective studies [1, 3]. Additionally, early mortality within 3 days in CAP only rarely has been studied so far [3–5]. The aim of the present analysis was to characterise patients dying within 3 days after hospitalisation for CAP using the unique database of the German nationwide mandatory quality assurance programme, which requests all hospitals in Germany to document all cases hospitalised with CAP according to a pre-specified electronic data sheet.

For this study, data from the 5-year period between 2009 and 2013 were included. Cases with CAP were identified by a set of International Classification of Diseases codes as listed elsewhere [1]. Comorbidity was not included in the analysis since it is not consistently documented in all patients and because there are no data on its severity. In addition, there are no data on Do Not Resuscitate orders or causes of death. The primary outcome parameter was death within 3 days after hospital admission. The CRB-65 (confusion, respiratory rate $\geqslant$30 breaths per min, systolic blood pressure <90 mmHg or diastolic blood pressure $\leqslant$60 mmHg) and age $\geqslant$65 years) score was determined as described previously [6]. After 2010, respiratory rate was not a mandatory field to be recorded; cases with missing respiratory rate were considered normal. For univariate analyses, continuous variables were compared using Student's t-test and categorical variables using the Chi-squared test. To evaluate the independent association of predictive parameters with 3-day mortality, a multivariate logistic regression model with stepwise forward selection was performed. Risk factors included were the CRB-65 criteria and mechanical ventilation on admission. Receiver operating characteristic (ROC) curve analysis was used to determine the diagnostic properties of the CRB-65 score.

A total of 1 195 461 patients with hospitalised CAP were documented in Germany between 2009 and 2013. Of those, 49 538 patients transferred from other hospitals were excluded in order to avoid redundant documentation. The remaining 1 145 923 patients showed a hospital mortality of 13.1% (150 116 out of 1 145 923). Of these deaths, 38.6% (58 087) occurred within the first 3 days of hospitalisation (3-day mortality 5.1%).

In order to overcome the problem of treatment restrictions in patients already severely compromised before the CAP episode, patients who were either bedridden prior to admission and/or residing in a nursing home, and/or not receiving antibiotic treatment (366 207 cases; 3-day mortality 10.8%, hospital mortality 25.7%) were excluded from the analysis. The remaining 779 716 patients showed a 3-day mortality of 2.4% (18 474 deaths), corresponding to 33% of all in-hospital deaths (56 250; hospital mortality 7.2%). Characteristics of these patients are shown in table 1. Age, sex and the CRB-65 criteria were significantly associated with 3-day mortality. In patients with mechanical ventilation, the 3-day mortality rate was 8.6%, as compared to 1.9% in patients without mechanical ventilation (p<0.001). However, of the patients dying within 3 days, only 23.3% had received mechanical ventilation before. In multivariate analysis, mechanical ventilation on admission showed the highest risk of 3-day mortality. Additionally, all CRB-65 criteria were independently associated with 3-day mortality, with pneumonia-related confusion showing the highest risk. 3-day mortality increased with each CRB-65 point and was 0.6% in CRB-65 0, 1.9% in CRB-65 1, 4.2% in CRB-65 2, 10.4% in CRB-65 3 and 20.9% in CRB-65 4. After ROC analysis, the CRB-65 score showed an area under the curve (AUC) of 0.69 (95% CI 0.68–0.69, p<0.001) for predicting 3-day mortality. Optimal cut-off according to the Youden index was two or more criteria (sensitivity 51.3%, specificity 77.7%). A score of 0 showed a negative predictive value of 99.4% (negative likelihood ratio 0.27), whereas scores of three or more and four criteria had positive predictive values of 11.4% (positive likelihood ratio 5.25) and 20.9% (positive likelihood ratio 10.0), respectively.

The main strength of our findings lies in the evaluated database virtually excluding any selection bias by including all German hospitalised CAP patients, thus allowing an unparalleled, scientifically and educationally important insight into epidemiology and the often underestimated emergency presentation of CAP. Our data demonstrate that there is a relevant subgroup of CAP patients dying within 3 days of hospital admission, even after exclusion of patients with poor functional status, nursing home residents and those not receiving

TABLE 1 Characteristics of patients and multivariate regression analysis including CRB-65 criteria and mechanical ventilation on admission according to 3-day mortality

Characteristic	Univariate analysis			Multivariate analysis	
	3-day nonsurvivors	3-day survivors	p-value	OR (95% CI)	p-value
Patients n	18 474	761 242			
Demographics					
Age years	77.8±11.7	69.5±16.5	<0.001		
Male sex	11 189 (60.6)	443 267 (58.2)	<0.001		
CRB-65 criteria					
Age ⩾65 years	16 063 (86.9)	533 548 (70.1)	<0.001	2.43 (2.33–2.54)	<0.001
Pneumonia-related confusion	3973 (21.5)	44 243 (5.8)	<0.001	3.48 (3.35–3.61)	<0.001
Respiratory rate ⩾30 breaths per min	3819 (20.7)	68 085 (8.9)	<0.001	2.28 (2.20–2.37)	<0.001
Blood pressure <90/⩽60 mmHg	6610 (35.8)	135 050 (17.7)	<0.001	2.40 (2.33–2.48)	<0.001
CRB-65 score	1.65±0.89	1.03±0.75	<0.001		
0	1146 (6.2)	176 464 (23.2)			
1	7851 (42.5)	414 839 (54.5)			
2	6365 (34.5)	145 803 (19.2)			
3	2564 (13.9)	22 063 (2.9)			
4	548 (3.0)	2073 (0.3)			
MV					
On admission	940 (5.1)	7671 (1)	<0.001	9.09 (8.46–9.76)	<0.001
At all	4296 (23.3)	45 417 (6.0)	<0.001		
Invasive only	2192 (11.9)	12 358 (1.6)			
Noninvasive only	1342 (7.3)	19 400 (2.5)			
Both	762 (4.1)	13 659 (1.8)			

Data are presented as mean±SD or n (%), unless otherwise stated. MV: mechanical ventilation.

antibiotic treatment to avoid bias due to possible treatment restrictions. The resulting 3-day mortality rate of 2.4% is higher than that reported by two recent populations from prospective studies evaluating this end-point [3, 4] and still high when compared to the reported 48-h mortality rate of 2.3% in a study including all patients with CAP in a Spanish hospital without excluding nursing home or bedridden patients [5]. For Germany, this means that nearly 3700 of these patients per year are affected. This has implications for planning and evaluating possible interventions in order to improve management of these patients.

Our mechanical ventilation rate before death on day 3 of only 23.3%, even after exclusion of patients who were bedridden or residing in a nursing home, matches that of a recent analysis of this database and could reflect either treatment restrictions or deficient clinical performance [7].

As far as we know, no other study evaluated the CRB-65 score for 3-day mortality so far. Our data demonstrate that the negative predictive value of a CRB-65 of 0 was very high (99.4%). However, even this favourable performance implies that 1146 patients not being bedridden or coming from a nursing home with a score of 0 died within 3 days in Germany during the 5-year study period. Additionally, the AUC of 0.69 for prediction of 3-day mortality in our database was lower than that reported by recent studies and meta-analyses for hospital mortality [8, 9], which might reflect a poorer performance of this score for this early outcome. Strategies that may reduce the risk of early death despite a low CRB-65 score include evaluation of sepsis- or comorbidity-related organ dysfunction, including oxygenation and other proposed parameters like the American Thoracic Society/Infectious Diseases Society of America (ATS/IDSA) minor criteria [10–13]. Moreover, patients should be clinically assessed repeatedly during the first 3 days of hospitalisation [14, 15].

Several limitations of our study have to be mentioned. The interpretation of our findings is limited by the lack of data on other important risk factors and management parameters like comorbidities, microbiology, intensive care unit admission, appropriateness of antimicrobial therapy, course of deterioration of patients and treatment restrictions, as valid information on these parameters cannot be retrieved from the quality performance programme. In addition, we cannot provide data on causes of death. Finally, other proposed risk scores like the Pneumonia Severity Index or the ATS/IDSA minor criteria are not available from the database. However, the coverage of virtually all hospitalised CAP patients in Germany reflects real-world management and minimises selection bias. Moreover, data completeness of the predefined outcome parameters as well as the CRB-65 score makes the evaluated database unique within the published CAP research.

In conclusion, we found a high 3-day mortality rate of 2.4% (one-third of all in-hospital deaths) in a large cohort of hospitalised CAP patients who were not bedridden or residing in nursing homes. The CRB-65

score showed a high negative predictive value for early death. Patients presenting with severity criteria should be carefully evaluated for sepsis- or comorbidity-related acute organ dysfunction.

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3-day mortality from CAP corresponds to 33% of in-hospital deaths; the CRB-65 criteria are independent predictors http://ow.ly/XFMlB

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