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Why Do Nonsurvivors from Community-Acquired Pneumonia Not Receive Ventilatory Support?

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Abstract
Objective We investigated rates and predictors of ventilatory support during hospitalization in seemingly not severely compromised nonsurvivors of community-acquired pneumonia (CAP).
Methods We used the database from the German nationwide mandatory quality assurance program including all hospitalized patients with CAP from 2007 to 2011. We selected a population not residing in nursing homes, not bedridden, and not referred from another hospital. Predictors of ventilatory support were identified using a multivariate analysis.
Results Overall, 563,901 patients (62.3 % of the whole population) were included. Mean age was 69.4 ± 16.6 years; 329,107 (58.4 %) were male. Mortality was 39,895 (7.1 %). A total of 28,410 (5.0 %) received ventilatory support during the hospital course, and 76.3 % of nonsurvivors did not receive ventilatory support (62.6 % of those aged <65 years and 78 % of those aged ≥65 years). Higher age (relative risk (RR) 0.48, 95 % confidence interval (CI) 0.44–0.51), failure to assess gas exchange (RR 0.18, 95 % CI 0.14–0.25) and to administer antibiotics within 8 h of hospitalization (RR 0.48, 95 % CI 0.39–0.59) were predictors of not receiving ventilatory support during hospitalization. Death from CAP occurred significantly earlier in the nonventilated group (8.2 ± 8.9 vs. 13.1 ± 14.1 days; $p < 0.0001$).
Conclusions The number of nonsurvivors without obvious reasons for withholding ventilatory support is disturbingly high, particularly in younger patients. Both performance predictors for not being ventilated remain ambiguous, because they may reflect either treatment restrictions or deficient clinical performance. Elucidating this ambiguity will be part of the forthcoming update of the quality assurance program.

Keywords Pneumonia · Outcome · Mechanical ventilation · Noninvasive ventilation · Mortality

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Abbreviations

CAP	Community-acquired pneumonia
CRB-65	Severity score (c = pneumonia-related confusion, r = respiratory rate ≥30/min, b = blood pressure <90 mm systolic and ≤60 mmHg diastolic, 65 is age ≥65 years)
ICD	International classification of diseases

Several recent studies demonstrate that mortality from community-acquired pneumonia (CAP) is still considerably high, varying between 4.3 and 22.6 % [1]. The high range of mortality rates evidently depends on the characteristics of the populations, including age, comorbidity, and severity [2, 3]. Compared with cardiovascular events, such as acute coronary syndrome, these mortality rates seem excessively high.

Studies evaluating clinical pathways and standards according to guidelines to reduce mortality in patients with CAP have shown an improvement in clinical outcomes, particularly mortality [4, 5]. However, compared with the magnitude of interventions to lower mortality in cardiovascular conditions, such as acute coronary syndrome and stroke, no comparable effort has been made in patients with CAP [6].

One major problem in intervention studies to improve the outcomes of patients with CAP is the failure to account for the large amount of patients with CAP and treatment restrictions for reasons of advanced age and severe comorbidity. This confounder is particularly but not exclusively relevant in studies, including patients with healthcare-associated pneumonia (HCAP) [7]. In fact, in a large recent study of patients with severe CAP, 33 % were excluded for reasons of treatment restriction [8]. Therefore, any strategy to reduce mortality should focus on the subgroup of patients which will probably benefit from intensified treatment. Excluding patients with typical risk factors for treatment restrictions, such as nursing home residency and not being bedridden, most patients with severe CAP should be candidates for such treatment. A relevant number of nonsurvivors of CAP not ventilated could hint at a failure to administer ventilatory support (noninvasive and/or invasive) appropriately and timely.

The large database of the German nationwide mandatory quality assurance program offers the opportunity to study the amount of nonsurvivors from CAP without such typical risk factors for treatment limitations but not receiving ventilatory support during hospitalization and to investigate predictors of ventilatory support.

Methods

Database

The database comprises data from the German nationwide mandatory quality assurance program launched in 2005, which obliges all hospitals in Germany to document all cases hospitalized with CAP according to a prespecified data sheet. The sheet was elaborated by a scientific working group. Cases with CAP were identified by a set of ICD codes as listed elsewhere [3]. Patients investigated in the emergency room but not hospitalized were not recorded. Comorbidity was not included in the analysis since comorbidity was not a mandatory field and not consistently documented in all patients, and because there were no data on its severity. Also, there were no data on DNR orders and reasons of death.

For the purpose of this investigation, the most recent data from a 4-year period (2007–2011) were included. Since blood urea nitrogen is rarely determined in Germany and not required in the performance program, severity of CAP was classified according to the CRB-65 score. Ventilatory support included noninvasive and invasive ventilation. Failure to provide ventilatory support was defined as a failure to provide noninvasive and/or invasive ventilation at any time after hospital admission until discharge or death.

Patient Population

Overall, the database included 904,551 patients. In view of the study hypothesis patients being mechanically ventilated at admission were not included ($n = 17{,}092$; 1.9 %). The baseline population of interest was the seemingly not severely compromised, i.e., that without characteristics frequently associated with treatment limitations. Therefore, patients residing in nursing homes ($n = 198{,}239$; 21.9 %) and bedridden patients ($n = 217{,}150$; 24 %) were excluded. In addition, patients referred from other hospitals were excluded to avoid doubling of cases ($n = 39{,}178$; 4.3 %). Since 2011, respiratory rate was not a mandatory file to be recorded; therefore, cases with missing data also were not included ($n = 28{,}472$; 3.2 %). The resulting baseline population comprised 563,901 (62.3 %) patients.

The multivariate analyses of risk factors for predictors of ventilatory support during hospitalization (both invasive and noninvasive) included only patients ultimately dying during hospitalization ($n = 39{,}895$). Possible risk factors included in the multivariate model were: (1) basic characteristics (age, gender); (2) factors associated with severity of CAP (respiratory rate $\geq$30/min, hypotension (systolic pressure <90 mmHg or diastolic pressure $\leq$60 mmHg), pneumonia-related mental confusion; (3) factors that might reflect failures of process quality, i.e., performance markers (failure to assess blood gas exchange by pulse oximetry and/or blood gas analysis; failure to administer antimicrobial treatment within 8 h after hospital admission).

Multivariate analyses were performed in the whole population and repeated in patients aged <65 years.

Statistics

Data are reported as frequencies with percentages and mean ± SD. For univariate analyses, continuous variables were compared using Student's t test and categorical variables using the χ^2 test.

For multivariable analyses, we used a binary logistic regression model with stepwise forward selection

($p_{in} < 0.05$; $p_{out} > 0.1$). Results of this analysis are reported as odds ratio, 95 % confidence interval (95 % CI), and the level of significance. The odds ratio is a way of comparing whether the probability of a certain event is the same for two groups. Because women were overrepresented in the older age groups, we included an interaction term, including age and gender.

All multivariable analyses were repeated for the different types of ventilatory support (none versus invasive or invasive and noninvasive, and none versus noninvasive) and for patients younger 65 years to ensure stability of the set of predictors. In addition, we analyzed the data set for predictors for physicians' choice of ventilatory support.

A p value < 0.05 was reported as significant and exact p values are reported.

Results

Baseline Patient Population

The 563,901 patients had a mean age of 69.4 ± 16.6 years; 329,107 (58.4 %) were male, and 234,794 (41.6 %) female. Overall, 39,895 (7.1 %) died, and 28,410 (5.0 %) received ventilatory support during the hospital course. The baseline clinical characteristics of the total population and those aged <65 and ≥65 years are provided in Table 1.

Elderly patients aged ≥65 years had higher CRB-65 scores and significantly more frequently CRB-65 severity criteria. In contrast, younger patients had a slightly but significantly higher proportion of failures to comply with both process markers.

Patients received ventilatory support equally frequently in both age groups (5 %). However, ventilatory rates were lower at the extremes of age (20–29 years, 2.7 %; 30–39, 2.6 %; 40–49, 4.4 %; 50–59, 6 %; 60–69, 6.5 %; 70–79, 5.9 %; 80–89, 4.3 %; 90–99, 1.7 %; and >100, 0.8 %).

Mortality was more than thrice as high in elderly patients (2.6 vs. 9 %).

The clinical characteristics of nonsurvivors not ventilated ($n = 39{,}895$) is provided in Table 2. Younger patients had more frequently high respiratory rates and hypotension but less frequently pneumonia-related confusion. There was no difference with regard to failures to comply with both failure markers. Younger patients were more frequently ventilated than elderly (37.4 vs. 22 %).

In patients who died during hospitalization, mean survival time was 9.3 ± 10.5 days. In patients who received ventilatory support before death, mean survival was 13.1 ± 14.1 days, whereas it was 8.2 ± 8.9 days ($p < 0.0001$) not receiving it. These figures translated into 11.9 ± 13.9 versus 7.3 ± 8.7 days in those aged <65 years ($p < 0.0001$), and 13.3 ± 14.1 versus 8.2 ± 8.9 in the elderly group ($p < 0.0001$). Thus, patients without ventilatory support died earlier in the course of the disease, with the highest risk within the first 48 h after admission (Fig. 1).

Predictors of Ventilatory Support in Patients with Lethal Outcome

As expected, high respiratory rate, hypotension, and pneumonia-related mental confusion predicted ventilatory support. Age, female gender, and failure to assess blood gas exchange by pulse oximetry and/or blood gas analysis as well as failure to administer antimicrobial treatment within 8 h after hospital admission were predictive of not receiving ventilatory support. After inclusion of the interaction term age for gender, gender was no longer predictive of such failure, because women were overrepresented in the older age groups (Table 3).

When this analysis was repeated for the different types of ventilatory support, no substantial changes in predictors and/or magnitude of effect were noted in the invasive mechanical ventilation subanalysis (Table 4). In the subanalysis of patients receiving only noninvasive mechanical ventilation, age >65 years and low blood pressure were no longer predictive.

The multivariate analysis for the younger patients (aged <65 years) confirmed the similar set of predictors (Table 5).

Discussion

The main findings of this investigation are the following: (1) a significant proportion of nonsurvivors of CAP seemingly not severely compromised, i.e., without typical risk factors for treatment limitation did not receive ventilatory support (76.3 %), both noninvasive and invasive; (2) this was also true for younger patients (62.6 %); (3) higher age and failure to assess gas exchange and to administer antibiotics within 8 h of hospitalization were predictors of not receiving ventilatory support during hospitalization; (4) nonsurvivors without ventilatory support died significantly earlier than those receiving it.

In a previous investigation based on the quality assurance database from 2005 to 2006, we could show that residing in nursing homes and being bedridden were the conditions with the highest associated risk of death in patients with CAP, with relative risks of 2.3 and 3.7, respectively [3]. Accordingly, excluding patients with these conditions reduced the risk of death from approximately 14 to 7.6 % in that investigation and 7.1 % in this series, a mortality rate well in the range of that reported in many studies of CAP [1]. We additionally excluded those transferred from other hospitals to avoid doubling of

Table 1 Clinical characteristics of the selected baseline population with CAP (n = 563,901)

Variable	Total population	Age <65 years	Age ≥65 years	p
Age, n (±)	69.4 (16.6)	48.3 (12.2)	78.4 (7.5)	<0.0001
Gender (m/f)	329,107 (58.4 %)/234,794 (41.6 %)	98,992 (58.7 %)/69,679 (41.3 %)	230,115 (58.2 %)/165115 (41.8 %)	<0.001
Respiratory rate ≥30/min	58,431 (10.4 %)	15,463 (9.2 %)	42,968 (10.9 %)	<0.0001
Systolic blood pressure <90 mmHg or diastolic blood pressure ≤60 (mmHg)	102,979 (18.3 %)	26,224 (15.5 %)	76,755 (19.4 %)	<0.0001
Pneumonia-related confusion, n (%)	36,634 (6.5 %)	4,861 (2.9 %)	31,773 (8.0 %)	<0.0001
CRB-65				<0.0001
0	127,480 (22.6 %)	127,480 (75.6 %)	–	
1	303,480 (53.8 %)	36,332 (21.5 %)	267,148 (67.6 %)	
2	111,279 (19.7 %)	4,361 (2.6 %)	106,918 (27.1 %)	
3	19,412 (3.4 %)	498 (0.3 %)	18,914 (4.8 %)	
4	2,250 (0.4 %)	–	2,250 (0.6 %)	
Failure to determine initial gas exchange, n (%)	20,087 (3.6)	6,497 (3.9)	13,590 (3.4)	<0.0001
Failure to administer antimicrobial treatment within 8 h after admission not achieved	8,281 (1.5 %)	3,125 (1.9 %)	5,156 (1.3 %)	<0.0001
Ventilatory support (noninvasive and/or invasive)	28,410 (5.0 %)	8,455 (5.0 %)	19,955 (5.0 %)	0.29
Only invasive	7,781 (1.4 %)	2,445 (1.4 %)	5,336 (1.4 %)	<0.0001
Only noninvasive	12,388 (2.2 %)	3,337 (2.0 %)	9,051 (2.3 %)	
Invasive and noninvasive at any time	8,241 (1.5 %)	2,673 (1.6 %)	2,673 (1.6 %)	
Mortality, n (%)	39,895 (7.1)	4,411 (2.6)	35,484 (9.0)	<0.0001

patients. A further step to reduce the amount of patients with potentially futile prognosis would have been to include and to weigh comorbidity. Unfortunately, the ICD codes of mortality were not a mandatory field to complete; these data will not be available before 2013. Even so, we thought that our selected population was uncompromised enough to be potentially subject to treatment escalation. Although acute respiratory failure might not be present in all patients dying from CAP, we thought it would be reasonable to use ventilatory support as a surrogate for such escalation.

As expected, severity criteria were predictive of receiving ventilatory support in nonsurvivors, whereas higher age was negatively associated with such intervention. This finding increases confidentiality with the validity of the database. However, the rates of not being ventilated in nonsurvivors was disturbingly high, reaching 76.3 % in the whole population, and 62.6 % of those aged <65 years and 78 % of those aged ≥65 years. There is little doubt that a proportion of patients, although younger and/or self-sufficient or not bedridden probably was subject to treatment restriction due to comorbidities not identified in this

Table 2 Clinical characteristics of the selected population with CAP with lethal outcome ($n = 39{,}895$)

Variable	Total population	Age <65 years	Age ≥65 years	p
Age, n (±)	78.0 (11.0)	55.8 (7.2)	80.7 (7.7)	<0.0001
Gender (m/f)	24,996 (62.7 %)/14,899 (37.3 %)	3,060 (69.4 %)/1,351 (30.6 %)	21,936 (61.8 %)/13,548 (38.2 %)	<0.0001
Respiratory rate ≥30/min	8,079 (20.3 %)	1,032 (23.4 %)	7,047 (19.9 %)	<0.0001
Systolic blood pressure <90 mmHg or diastolic blood pressure ≥60 (mmHg)	12,744 (31.9 %)	1,498 (34.0 %)	11,246 (31.7 %)	<0.002
Pneumonia-related confusion, n (%)	7,633 (19.1)	657 (14.9)	6,976 (19.7)	<0.0001
CRB-65				<0.0001
0	2,065 (5.2 %)	2,065 (46.8 %)	–	
1	18,442 (46.2 %)	1,623 (26.9 %)	16,814 (47.4 %)	
2	13,660 (34.2 %)	595 (13.5 %)	13,065 (36.8 %)	
3	4,734 (11.9 %)	123 (2.8 %)	4,611 (13.0 %)	
4	9,904 (2.5 %)	–	994 (2.8 %)	
Failure to determine initial gas exchange, n (%)	1,307 (3.3)	140 (3.2)	1,167 (3.3)	0.72
Failure to administer antimicrobial treatment within 8 h after admission, n (%)	1,017 (2.5)	110 (2.5)	907 (2.6)	0.84
Ventilatory support (noninvasive and/or invasive)	9,448 (23.7 %)	1,650 (37.4 %)	7,798 (22.0 %)	<0.0001
Only invasive	3,843 (9.6 %)	794 (18 %)	3,049 (8.6 %)	<0.0001
Only noninvasive	2,520 (6.3 %)	277 (6.3 %)	2,243 (6.3 %)	
Invasive and noninvasive at any time	3,085 (7.7 %)	579 (13.1 %)	2,506 (7.1 %)	

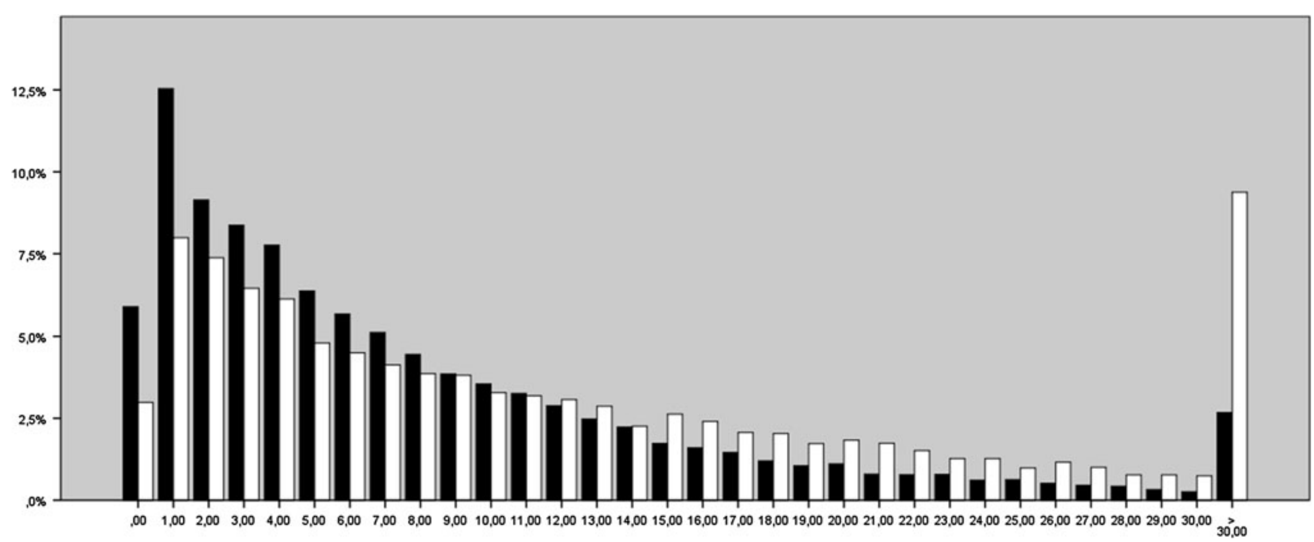

Fig. 1 Time of death in nonsurvivors of CAP, stratified into those without and with ventilatory support (both noninvasive and invasive) during hospitalization. *Black bars* nonsurvivors without ventilatory support; *white bars* nonsurvivors with ventilatory support

Table 3 Multivariate analysis of predictors for receiving ventilatory support (noninvasive, invasive or both) in patients with CAP and lethal outcome ($n = 39{,}895$)

Variable	Risk ratio	95 % confidence interval	p
Age ≥65 years	0.66	0.59–0.72	<0.0001
Age by gender (interaction term)	0.78	0.74–0.83	<0.0001
Respiratory rate ≥30/min	1.75	1.66–1.85	<0.0001
Systolic blood pressure <90 mmHg or diastolic blood pressure ≤60 (mmHg)	1.07	1.02–1.12	0.009
Pneumonia-related confusion	1.27	1.2–1.35	<0.0001
Failure to determine initial gas exchange	0.18	0.14–0.24	<0.0001
Failure to administer antimicrobial treatment within 8 h after admission	0.48	0.4–0.59	<0.0001

Table 4 Multivariate analysis of predictors for receiving mechanical support analyzed separately for noninvasive and/or invasive mechanical ventilation in patients with CAP and lethal outcome ($n = 39{,}895$)

Variable	Noninvasive ($n = 2{,}520$)			Noninvasive and/or invasive ($n = 6{,}928$)		
	RR	95 % confidence interval	p	RR	95 % confidence interval	p
Age ≥65 years	–	–	–	0.59	0.53–0.66	<0.0001
Age by gender (interaction term)	0.85	0.8–0.91	<0.0001	0.75	0.71–0.8	<0.0001
Respiratory rate ≥30/min	1.86	1.69–2.03	<0.0001	1.72	1.62–1.83	<0.0001
Systolic blood pressure <90 mmHg or diastolic blood pressure ≤60 (mmHg)	–	–	–	1.07	1.01–1.13	0.021
Pneumonia-related confusion	1.34	1.21–1.47	<0.0001	1.23	1.17–1.34	<0.0001
Failure to determine initial gas exchange	0.16	0.1–0.27	<0.0001	0.19	0.14–0.25	<0.0001
Failure to administer antimicrobial treatment within 8 h after admission	0.36	0.24–0.55	<0.0001	0.52	0.42–0.65	<0.0001

Table 5 Multivariate analysis of predictors for not receiving ventilatory support (noninvasive and/or invasive) in patients nonsurvivors with CAP aged <65 years ($n = 4{,}406$)

Variable	RR	95 % confidence interval	p
Respiratory rate ≥30/min	2.07	1.79–2.39	<0.0001
Systolic blood pressure <90 mmHg or diastolic blood pressure ≤60 (mmHg)	1.18	1.03–1.34	0.02
Pneumonia-related confusion	1.61	1.36–1.92	<0.0001
Failure to determine initial gas exchange	0.18	0.1–0.32	<0.0001
Failure to administer antimicrobial treatment within 8 h after admission	0.43	0.26–0.71	<0.001

program, dementia being a prominent example [9]. Nevertheless, this explanation seems implausible for a large amount of patients.

We identified two process markers (determination of initial gas exchange and administration of antimicrobial treatment within 8 h) as being associated with not receiving ventilatory support in nonsurvivors. Unfortunately, these parameters remain ambiguous with regard to reasons underlying the decision to withhold ventilatory support. The failure to comply with these two markers may reflect both treatment restrictions as well as severely deficient clinical performances, including a failure to recognize indications for ventilatory support.

In any case, initial gas exchange should be assessed also in patients judged to have a futile prognosis, and a failure to do so does reflect a deficient quality. Although processes of care are not necessarily directly related to outcomes and particularly mortality [10], the failure to comply with these processes has been repeatedly been reported to be associated with adverse clinical outcomes [11–13].

The interpretation of our findings is limited by the lack of data on specific comorbidities, DNR orders, and reasons of death. Valid information on specific comorbidities is difficult to retrieve within such a performance program. However, given the selection criteria of our population, the comorbidities associated with the highest risk of treatment restrictions and ultimately death were excluded. Also, simply relying on DNR orders might not be enough. Although it has been described that most in-hospital pneumonia deaths occur in patients who have a DNR order, with early DNRs reflecting comorbidity and late also the futility of care [14], DNR orders might not reflect the whole spectrum of possible treatment restrictions. In addition, including DNR orders as mortality risk adjustment might introduce important bias in performance reporting [15]. Finally, reasons of death are difficult if not impossible to determine in such a large patient population. On the other hand, deaths in the younger population might not be preventable [16]. Overall, because most deaths ultimately are preceded by respiratory failure might not be useful to elucidate why ventilator support was not provided.

Nevertheless, the principal ambiguity of our results must urgently be resolved. Therefore, the scientific group of the quality program decided to introduce into the next update four additional questions in every case patient who died without having received ventilatory support: (1) Was there any treatment restriction related to comorbidity?; (2) Did the patient deny ventilatory support?; (3) Did the patient die from an unexpected clinical event?; (4) Was there a lack of ventilation facilities? Such a short list of questions seems a more adequate approach to catch a realistic reflection of routine practices in such a delicate area of performance measurement.

The first question offers the opportunity to balance such statement of treatment restrictions with comorbidities present. The second takes account to the ever increasing relevance of patients' preferences. The third records unexpected cases of death that might occur, e.g., as a consequence of lethal cardiovascular events, which are increasingly recognized a prominent cause of nonpneumonia-related death [17–19]. Such unexpected event also might have been prevented, and compliance with standards of care might improve the recognition of patients at risk [20, 21]. Finally, the forth question reveals a frankly unacceptable situation, which needs to be corrected urgently.

Germany provides a high number of adult ICU beds (24.0/100,000 inhabitants) and has been shown to have a high volume of ICU admissions per year (2,353/100,000 inhabitants) [22]. A high inverse correlation between ICU beds and hospital mortality for intensive care unit patients across countries has been identified [22]. Therefore, rationing critical care beds should not be an issue in Germany [23]. Overall, there should be no reason to withhold ventilatory support other than well-documented medical futility.

We ignore to what extent these findings are relevant for other European and non-European countries since to the best of our knowledge no comparable investigations have been published so far. However, given the fact that the incidence and mortality rates of CAP are comparable [24] and that in contrast to other countries there is obviously no shortcoming in ICU beds in Germany, similar if not more serious results could be expected in other countries. Therefore, it would be prudent to investigate the rate of ventilatory support in nonsurviving CAP patients in routine practice also in other countries.

In fact, a reason behind a failure to provide ventilatory support may be an underestimation of the hazards inherent to CAP [17–20]. In that case, recognizing CAP, as an emergency and implementing a structured intervention plan comparable to cardiovascular emergencies would be a high clinical and political priority [6].

In conclusion, the large amount of seemingly not severely compromised nonsurvivors of CAP not receiving ventilatory support without being able to explain the reasons behind such restraint hints at a major problem in clinical performance and/or in performance measurement in German hospitals. The update of the performance program will elucidate the inherent ambiguities of the associated failure to comply with two performance markers. In the meantime, available risk scores should be used to identify patients with severe pneumonia requiring intensified treatment [2, 8].

Key Messages

1. A disturbingly large proportion of nonsurvivors of hospitalized CAP in Germany seemingly not severely compromised do not receive ventilatory support during the course of hospitalization (76.3 %, and still 62.3 % of those aged <65 years).
2. Failure to achieve two performance predictors within the national German quality assurance program was associated with failure to provide ventilator support in these patients.
3. Although treatment restrictions might account for a part of these failures, these data might hint at a major problem in the management of patients with CAP and should urge prospective evaluation of reasons for not providing ventilator support.

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Conflict of interest The authors declare that they have no competing interests.

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