ORIGINAL INVESTIGATION

Causes of Death for Patients With Community-Acquired Pneumonia

Results From the Pneumonia Patient Outcomes Research Team Cohort Study

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Background: To our knowledge, no previous study has systematically examined pneumonia-related and pneumonia-unrelated mortality. This study was performed to identify the cause(s) of death and to compare the timing and risk factors associated with pneumonia-related and pneumonia-unrelated mortality.

Methods: For all deaths within 90 days of presentation, a synopsis of all events preceding death was independently reviewed by 2 members of a 5-member review panel (C.M.C., D.E.S., T.J.M., W.N.K., and M.J.F.). The underlying and immediate causes of death and whether pneumonia had a major, a minor, or no apparent role in the death were determined using consensus. Death was defined as pneumonia related if pneumonia was the underlying or immediate cause of death or played a major role in the cause of death. Competing-risk Cox proportional hazards regression models were used to identify baseline characteristics associated with mortality.

Results: Patients (944 outpatients and 1343 inpatients) with clinical and radiographic evidence of pneumonia were enrolled, and 208 (9%) died by 90 days. The most frequent immediate causes of death were respiratory failure (38%), cardiac conditions (13%), and infectious conditions (11%); the most frequent underlying causes of death were neurological conditions (29%), malignancies (24%), and cardiac conditions (14%). Mortality was pneumonia related in 110 (53%) of the 208 deaths. Pneumonia-related deaths were 7.7 times more likely to occur within 30 days of presentation compared with pneumonia-unrelated deaths. Factors independently associated with pneumonia-related mortality were hypothermia, altered mental status, elevated serum urea nitrogen level, chronic liver disease, leukopenia, and hypoxemia. Factors independently associated with pneumonia-unrelated mortality were dementia, immunosuppression, active cancer, systolic hypotension, male sex, and multilobar pulmonary infiltrates. Increasing age and evidence of aspiration were independent predictors of both types of mortality.

Conclusions: For patients with community-acquired pneumonia, only half of all deaths are attributable to their acute illness. Differences in the timing of death and risk factors for mortality suggest that future studies of community-acquired pneumonia should differentiate all-cause and pneumonia-related mortality.

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PNEUMONIA COMBINED with influenza is the sixth leading cause of death in the United States.[1] Although the mortality rate from pneumonia decreased sharply with the introduction of antibiotic therapy in the 1940s, since 1950, the overall mortality rate for this illness has either remained stable or increased.[2] In a meta-analysis[3] of studies of prognosis, the short-term mortality of patients hospitalized with community-acquired pneumonia ranged from 5.1% for patients treated in an ambulatory or hospital setting to 36.5% for patients treated in an intensive care unit.

Prior studies[4-6] of pneumonia prognosis focused almost exclusively on short-term mortality and assessed risk factors for all-cause mortality. To our knowledge, no previous studies have examined the causes of death of patients with community-acquired pneumonia or the role that pneumonia played in the cause of death. The goals of this study were as follows: (1) to identify the underlying and immediate causes of death for patients with community-acquired pneumonia, (2) to determine the role that community-acquired pneumonia played in the cause of death, and (3) to compare the risk factors associated with pneumonia-related and pneumonia-unrelated mortality in patients with this illness.

RESULTS

Of the 2287 patients enrolled in the Pneumonia Patient Outcomes Research Team cohort study, 208 (9%) died within 90

PATIENTS AND METHODS

PATIENT RECRUITMENT

The Pneumonia Patient Outcomes Research Team cohort study was conducted at 5 medical institutions in 3 geographic locations between October 12, 1991, and March 31, 1994. These were the University of Pittsburgh Medical Center, a 942-bed university teaching hospital, and St Francis Medical Center, a 427-bed community teaching hospital, in Pittsburgh, Pa; Massachusetts General Hospital, an 899-bed university teaching hospital, and Harvard Community Health Plan–Kenmore Center, a staff-model health maintenance organization, in Boston, Mass; and Victoria General Hospital, a 637-bed university teaching hospital, in Halifax, Nova Scotia. Outpatients (defined as those initially treated in an outpatient setting) and inpatients were enrolled from each of the 4 hospital-based sites (University of Pittsburgh Medical Center, St Francis Medical Center, Massachusetts General Hospital, and Victoria General Hospital); only outpatients were enrolled from the Harvard Community Health Plan–Kenmore Center.

Potential study subjects were identified by research assistants through daily reviews of admitting and radiology department logs and records of patients presenting to the emergency departments and clinics affiliated with the participating sites. Inclusion criteria were as follows: 18 years of age or older, 1 or more symptoms suggestive of community-acquired pneumonia, radiographic evidence of community-acquired pneumonia not known to be chronic, and informed consent for baseline and follow-up interviews. Exclusion criteria were as follows: discharge from an acute-care facility within 10 days of presentation, known seropositivity for the human immunodeficiency virus, or pulmonary symptoms secondary to another diagnosis (eg, lung cancer). Patients were only enrolled once during the study; those who presented with community-acquired pneumonia on more than 1 occasion were not subsequently enrolled.

BASELINE ASSESSMENT

For all study patients, baseline sociodemographic information and clinical data were assessed at presentation by direct interview by a study nurse and medical record review. If unable to obtain information directly from the patient because of mental status changes or language or communication barriers, a proxy respondent was used. Clinical data examined included medical history, physical examination results, laboratory values, chest radiographic findings, and microbiologic results. Historical information obtained included 5 common respiratory symptoms (cough, dyspnea, sputum production, pleuritic chest pain, and hemoptysis) and 14 common nonrespiratory symptoms (fatigue, fever, anorexia, chills, sweats, headache, myalgias, nausea, sore throat, confusion, inability to eat, vomiting, diarrhea, and abdominal pain). Physical examination data collected included vital signs and an evaluation of mental status. Laboratory data collected, when available, included white blood cell count; hematocrit; levels of serum urea nitrogen, serum sodium, liver enzymes, and arterial blood gases; and pulse oximetry readings. Radiographic data included location of the infiltrate, pattern of the infiltrate (predominantly alveolar, predominantly interstitial, miliary, or mixed alveolar and interstitial), and presence of pleural effusion.

When ordered by the physicians caring for these patients, the following microbiologic tests were abstracted: sputum gram stains and bacterial cultures obtained within 2 days of presentation, blood cultures drawn before initiating antimicrobial therapy, pleural fluid cultures, and short-term (≤1 week of presentation) and convalescent (1-8 weeks after presentation) serologic tests. Results of these tests were reviewed and a microbiologic cause was assigned, as previously described.[7]

Copies of the initial chest radiographs used for the diagnosis of pneumonia at each study site were independently reviewed by a 3-member panel of attending radiologists who had no patient-specific clinical information. Pleural effusion was quantified by the maximum present in either lung as follows: none, minimal (costophrenic angle blunting only), moderate (less than one third of the pleural space), and large (one third or more of the pleural space).[8] Aspiration pneumonia was diagnosed by the clinical committee based on radiographic data and synopses of clinical data. Aspiration pneumonia was diagnosed in patients with a disorder known to alter consciousness, the normal gag reflex, or the swallowing mechanism in whom the chest radiograph revealed an infiltrate involving the superior or basilar segments of the lower lobes or the posterior segments of the upper lobes.[9]

The severity of illness at presentation was quantified using the validated Pneumonia Patient Outcomes Research Team prediction rule for 30-day mortality and medical complications in patients with community-acquired

days. Overall, 194 (14%) of the 1343 inpatients and 14 (1%) of the 944 outpatients died within this follow-up period.

CAUSES OF DEATH

As shown in **Table 1**, respiratory failure (38%), sepsis or bacteremia (7%), and cardiac arrhythmia (7%) were the 3 most frequent immediate causes of death. Neurological conditions (29%), lung cancer (13%), and cardiac ischemia (13%) were the 3 most frequent underlying causes of death.

Death was defined as pneumonia related in 110 (53%) of the 208 deaths. Of the pneumonia-related deaths, pneumonia was the underlying cause of death in 20 patients, the immediate cause of death in 9, and a major contributor to death in 81. Of the pneumonia-unrelated deaths, pneumonia played a minor role in 34 patients, no role in 52, and an unknown role in 12.

There were distinct differences between the immediate and underlying causes of death for pneumonia-related and pneumonia-unrelated mortality. The most frequent immediate causes of death for pneumonia-related mortality were respiratory failure (50%), pneumonia (8%), multisystem organ failure (6%), and sepsis (6%). In comparison, respiratory failure (26%), sepsis or bacteremia (9%), cardiac arrhythmia (8%), and congestive heart failure (7%) were the leading immediate causes of death for

pneumonia.[10] This rule is based on 3 demographic characteristics, 5 comorbid illnesses, 5 physical examination findings, and 7 laboratory and radiographic findings available at presentation. This rule classifies patients into 5 risk classes, with the 30-day mortality ranging from 0.1% for those in class I to 31.1% for those in class V.

ASSESSMENT OF MORTALITY AND THE CAUSE OF DEATH

Mortality was assessed at 90 days after initial enrollment in the study. For all patients who died during the follow-up period, death summaries were prepared by study research nurses using salient information obtained from the medical record, family or caregiver interviews, and autopsy reports (when available).

Each death summary was independently reviewed by 2 study investigators who were part of a 5-member clinical review panel (C.M.C., D.E.S., T.J.M., W.N.K., and M.J.F.). Four members of the clinical review panel were general internists (C.M.C., D.E.S., W.N.K., and M.J.F.) and 1 was an infectious disease specialist (T.J.M.); all reviewers had extensive clinical and research experience regarding patients with community-acquired pneumonia. The reviewers were asked to assign the underlying and immediate causes of death based on World Health Organization criteria,[11] and to assess the role that community-acquired pneumonia played in the patient's death. The underlying cause of death was defined as the disease or injury that initiated the cascade of morbid events leading directly to death. The immediate cause of death was defined as the disease process, injury, or complication immediately preceding death. If community-acquired pneumonia was not considered to be the underlying or immediate cause of death, then each reviewer was asked to determine whether community-acquired pneumonia played a major or a minor role in the patient's death. Pneumonia was judged as playing a major role if death would not have occurred if the patient did not have pneumonia but another condition was present that also contributed. Pneumonia was defined as playing a minor role if community-acquired pneumonia was not essential to explain the patient's death but played some role in the patient's death.

After the causes of death and the role of pneumonia in causing death were independently assigned by 2 reviewers, each case was presented to the 5-member clinical review panel. Final assignments of the underlying and immediate cause of death and the role of pneumonia in causing death were based on the full consensus of this panel.

Mortality was classified as pneumonia related if pneumonia was an immediate or underlying cause of death or if it played a major role in the patient's death. Mortality was defined as pneumonia unrelated if pneumonia was neither an immediate nor an underlying cause of death, and played only a minor role, no role, or an unknown role in the cause of death.

STATISTICAL ANALYSES

Univariate statistics were used to compare differences in sociodemographic and clinical characteristics in patients with pneumonia-related and pneumonia-unrelated mortality. Causes of death as a function of pneumonia severity risk class and timing of death were analyzed using simple descriptive techniques. Categorical variables were analyzed using the χ^2 test, and continuous variables were analyzed using the t test. To analyze time to death for patients with pneumonia-related and pneumonia-unrelated mortality, Kaplan-Meier estimated probabilities were computed. Statistical significance was assessed using the summary log-rank test. Statistical significance was defined as $P \leq .05$ (2-tailed) for all univariate and multivariate analyses.

To evaluate risk factors for pneumonia-related, pneumonia-unrelated, and all-cause mortality, baseline patient sociodemographic and clinical characteristics were used as independent variables in 3 Cox proportional hazards regression models, using the 3 mortality outcomes as the respective dependent measures. The baseline variables included all factors composing the Pneumonia Patient Outcomes Research Team severity model, in addition to others that were postulated to have an association with 90-day mortality.[10] Site of care, severity risk class, intensive care unit status, do not resuscitate status, and symptoms were omitted as potential predictors. All baseline variables that were statistically significant in any of the 3 Cox proportional hazards regression models were then used in a competing-risk Cox proportional hazards regression model with pneumonia-related mortality, pneumonia-unrelated mortality, and survival as the respective dependent measures.[12] The Kolmogorov-Smirnov test was used to test the statistical significance of the survival curves for pneumonia-related and pneumonia-unrelated mortality in the competing-risk analysis.[13]

pneumonia-unrelated mortality. The most frequent underlying causes of death for pneumonia-related mortality were neurological conditions (22%), pneumonia (18%), and cerebrovascular accident (13%), compared with lung cancer (19%), other malignancies (17%), and cardiac ischemia (17%) for those with pneumonia-unrelated mortality.

FACTORS ASSOCIATED WITH MORTALITY

The demographic and clinical factors with significant univariate associations with all-cause 90-day mortality are shown in **Table 2**. Overall, 85% of all deaths occurred among patients in the 2 highest risk classes; a greater proportion of pneumonia-related deaths also occurred within risk classes IV and V.

Survival plots and frequency distributions of death over time of pneumonia-related and pneumonia-unrelated mortality are shown in **Figure 1** and **Figure 2**. For the 110 pneumonia-related deaths, 45% occurred within 2 weeks and 76% occurred within 30 days of presentation, compared with 8% and 30%, respectively, of the pneumonia-unrelated deaths ($P < .001$ for both comparisons). The odds of a pneumonia-related death occurring within 30 days of presentation was 7.7 that of a pneumonia-unrelated death. The Kolmogorov-

Table 1. Immediate and Underlying Causes of Death for 208 Patients With Community-Acquired Pneumonia*

Cause of Death	Immediate Cause	Underlying Cause
Infectious	23 (11)	20 (10)
Pneumonia	9 (4)	20 (10)
Sepsis or bacteremia	14 (7)	0
Pulmonary, not pneumonia	81 (39)	21 (10)
Chronic lung disease†	0	20 (10)
Respiratory failure	80 (38)	0
Pulmonary embolus	1 (<1)	1 (<1)
Cardiac	27 (13)	30 (14)
Cardiac ischemia	1 (<1)	28 (13)
Cardiac arrhythmia	14 (7)	0
Congestive heart failure	12 (6)	0
Other cardiac cause	0	2 (1)
Neoplastic	2 (1)	50 (24)
Lung cancer	0	28 (13)
Other malignancy	2 (1)	22 (11)
Neurological conditions‡	8 (4)	61 (29)
Multisystem organ failure	8 (4)	0
Other conditions§	17 (8)	24 (12)
Unknown	42 (20)	2 (1)

*Data are given as number (percentage) of patients. Individual percentages may not sum to group totals because of rounding.
†Defined as 1 or more of the following: chronic obstructive pulmonary disease, interstitial or restrictive lung disease, and/or asthma.
‡Defined as 1 or more of the following: cerebrovascular accidents, amyotrophic lateral sclerosis, myasthenia gravis, multiple sclerosis, Parkinson disease, paraplegia, and/or quadriplegia.
§Including acute surgical abdomen, renal failure, liver disease, postoperative complications, rheumatologic disorders, diabetes mellitus, hemoptysis, peripheral vascular conditions, and depression.

Smirnov test confirmed significantly different patterns in the time to death for those with pneumonia-related and pneumonia-unrelated mortality ($P \leq .001$).

As shown in **Table 3**, 6 factors were independently associated with pneumonia-related mortality only: hypothermia, altered mental status, elevated serum urea nitrogen level, chronic liver disease, white blood cell count less than 4000/μL, and hypoxemia. In addition, 6 factors were associated with pneumonia-unrelated mortality only: dementia, immunosuppression, active cancer, systolic hypotension, male sex, and multilobar infiltrates. Two variables, increasing age and evidence of aspiration, were independently associated with pneumonia-related and pneumonia-unrelated mortality. The magnitude of association for the factors independently associated with pneumonia-related mortality only ranged from a hazard ratio of 1.90 for temperature lower than 36.0°C to 3.88 for chronic liver disease. The magnitude of association for the factors independently associated with pneumonia-unrelated mortality only ranged from 1.59 for male sex to 2.82 for dementia.

COMMENT

This detailed study of mortality in patients with community-acquired pneumonia demonstrates substantial differences in the causes, timing, and risk factors for pneumonia-related and pneumonia-unrelated deaths. The causes of death for patients in this study were similar to the most common causes of death for adults in the United States: coronary artery disease, malignancies, stroke, and chronic obstructive pulmonary disease.[14] The most frequent immediate causes of death in this study were respiratory failure and cardiac disease, while malignancies and neurological disorders were the most frequent underlying causes of death. However, several causes of death that many would associate with community-acquired pneumonia, including sepsis, bacteremia, and multisystem organ failure, were infrequent causes of death in this

Table 2. Factors Associated With All-Cause Mortality*

Factor	90-d Vital Status: Alive (n = 2079)	90-d Vital Status: Dead (n = 208)	P Value
Severity risk class			
I	769 (37)	3 (1)	
II	469 (23)	8 (4)	
III	306 (15)	20 (10)	<.01
IV	405 (19)	81 (39)	
V	130 (6)	96 (46)	
Demographic			
Male sex	1016 (49)	128 (62)	<.01
White race	1756 (84)	193 (93)	<.01
Nursing home resident	125 (6)	70 (34)	<.01
Signs			
Respirations ≥30/min	252 (12.1)	64 (30.8)	<.01
Heart rate ≥125 beats/min	171 (9.7)	29 (14.4)	.04
Systolic blood pressure <90 mm Hg	34 (1.9)	15 (7.4)	<.01
Temperature, °C			
<36.0	90 (4.9)	22 (11.2)	<.01
≥37.5	968 (53.1)	81 (41.3)	<.01
Altered mental status	157 (7.6)	81 (38.9)	<.01
Comorbid conditions			
Chronic lung disease†	519 (25.1)	69 (33.2)	.01
Coronary artery disease	337 (16.2)	69 (33.3)	<.01
Alcohol or other drug abuse	349 (19.3)	35 (32.7)	<.01
Cancer	234 (11.3)	60 (28.8)	<.01
Congestive heart failure	204 (9.8)	49 (23.7)	<.01
Neuromuscular disorder	194 (9.4)	49 (23.7)	<.01
Diabetes mellitus	198 (9.5)	37 (17.8)	<.01
Cerebrovascular disease	155 (7.5)	55 (26.4)	<.01
Immunosuppression	160 (7.8)	29 (14.0)	<.01
Renal disease	119 (5.7)	34 (16.4)	<.01
Dementia	89 (4.3)	52 (25.0)	<.01
Liver disease	28 (1.4)	5 (2.4)	.22
None listed	709 (35.5)	6 (2.9)	<.01
Laboratory and radiographic findings			
White blood cell count <4000/μL	26 (1.7)	9 (4.5)	.02
Hematocrit <30%	108 (7.2)	37 (18.3)	<.01
Serum urea nitrogen level >30 mg/dL (>10.7 mmol/L)	239 (18.3)	87 (44.4)	<.01
Arterial blood gas			
pH<7.35	60 (7.4)	24 (16.1)	<.01
Pco_2>45 mm Hg	100 (12.4)	37 (24.8)	<.01
Po_2<60 mm Hg	271 (33.4)	69 (46.3)	<.01
Arterial oxygen saturation <90%	192 (20.5)	58 (39.2)	<.01
Pleural effusion	168 (8.5)	36 (18.8)	<.01
Multilobar infiltrate	644 (37.1)	115 (66.5)	<.01
High-risk cause‡	133 (6.4)	83 (39.9)	<.01

*Data are given as number (percentage) of patients unless otherwise indicated.
†Defined as 1 or more of the following: chronic obstructive pulmonary disease, interstitial or restrictive lung disease, and/or asthma.
‡Defined as gram-negative rods, staphylococcus, aspiration pneumonia, or postobstructive pneumonia.

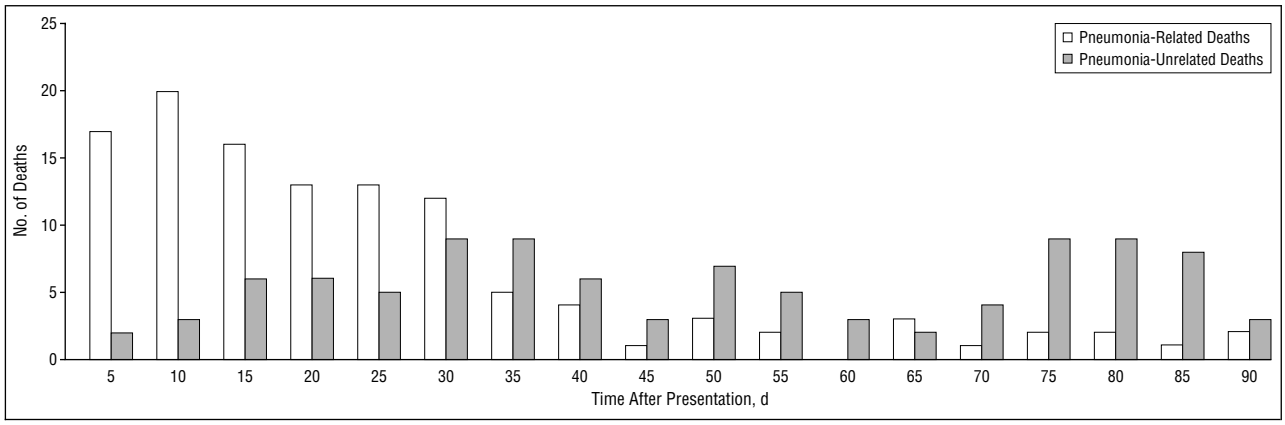

Figure 1. Frequency plot of pneumonia-related and pneumonia-unrelated mortality. Of the pneumonia-related deaths, 78% occurred within 30 days; of the pneumonia-unrelated deaths, 68% occurred after 30 days.

cohort. In addition, when the cause of death was stratified by the role of pneumonia, there were distinct differences between the 2 types of mortality. For patients with pneumonia-related mortality, the most frequent causes of death were respiratory failure and neurological disease, while for patients with pneumonia-unrelated mortality, the most frequent causes of death were malignancy and cardiac disease.

In this study, slightly more than half of the deaths were classified as pneumonia related, and more than 75% of the pneumonia-related deaths occurred within the first 30 days after presentation. After 30 days, the number of pneumonia-related deaths diminished rapidly, with less than 15% of all pneumonia-related deaths occurring after 45 days. In contrast, most pneumonia-unrelated deaths occurred between 30 and 90 days after presentation, with only 10% occurring within the first 2 weeks of presentation. These findings suggest that community-acquired pneumonia has a stronger association with mortality within 45 days of presentation and that prognosis beyond this point is more heavily influenced by the patient's age, sex, and other significant comorbid conditions.

We also found that the independent predictors of pneumonia-related and pneumonia-unrelated mortality were quite different. For pneumonia-unrelated mortality, comorbid conditions such as malignancy, immunosuppression, and dementia were independently associated with mortality. In contrast, chronic liver disease, a relatively rare condition, was the only comorbid condition independently associated with pneumonia-related mortality. In addition, for pneumonia-related mortality, acute physiologic or laboratory derangements, such as hypothermia, decreased white blood cell count, elevated serum urea nitrogen level, and hypoxemia, were independent predictors of mortality. For pneumonia-unrelated mortality, systolic hypotension was the only acute physiologic derangement associated with mortality. Increasing age and evidence of aspiration were the only risk factors associated with pneumonia-related and pneumonia-unrelated mortality. Increasing age is a significant risk factor for mortality, after community-acquired pneumonia, according to previous studies[3,15] of pneumonia prognosis. Aspiration events are related to multiple contributing factors that could affect prognosis, including neurological problems, malnutrition, and altered mental status.[16-18]

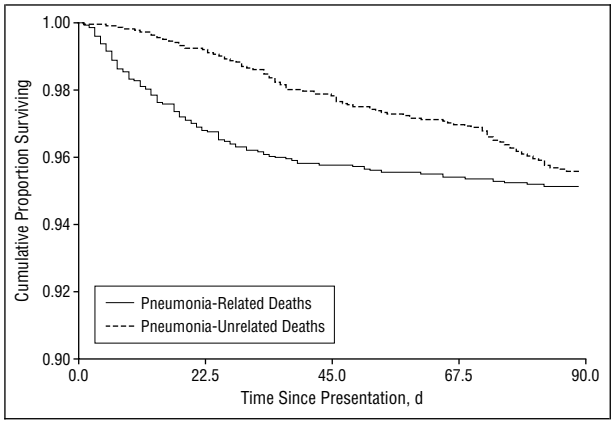

Figure 2. Survival plot of pneumonia-related and pneumonia-unrelated deaths.

There are several limitations of this work that should be acknowledged. First, approximately 130 patients who met study eligibility were not enrolled because of death before study enrollment. Therefore, this study may not reflect the full spectrum of patients who died within 90 days of community-acquired pneumonia. Second, the validity of using a clinical review committee to determine the cause of death for patients with community-acquired pneumonia has not been previously established. Although determining the cause of death by autopsy results represents the reference standard, autopsies were performed on only 22 of the patients who died, which limited our ability to assess the accuracy of the assignments of cause of death by the clinical committee. Nevertheless, this method was chosen because it was the most practical in nature and likely to provide more reliable data than death certificate reports. Similar clinical consensus methods have been used to classify mortality for many other conditions, such as cancer- and cardiac-related mortality.[19] Third, the accuracy of the case summaries was not independently confirmed by the physician investigations, which may have affected the assignments of the cause of death. Fourth, many outpatients had missing data for physical signs and laboratory values, which may have affected our analyses to determine factors associated with pneumonia-related and pneumonia-unrelated mortal-

Table 3. Factors Independently Associated With Pneumonia-Related or Pneumonia-Unrelated Mortality

Factor	Hazard Ratio (95% Confidence Interval)	
	Pneumonia-Related Mortality	Pneumonia-Unrelated Mortality
Age (per 10 y)	1.64 (1.39-1.93)*	1.28 (1.11-1.48)†
Male sex	1.48 (0.99-2.20)	1.59 (1.04-2.45)†
Heart rate >125 beats/min	1.58 (0.87-2.86)	1.75 (0.99-3.09)
Systolic hypotension (blood pressure <90 mm Hg)	1.28 (0.59-2.77)	2.63 (1.19-5.83)†
Hypothermia (temperature <36.0°C)	1.90 (1.03-3.49)*	1.59 (0.78-3.25)
Altered mental status	2.27(1.50-3.44)*	1.39 (0.86-2.27)
Active cancer	1.34 (0.82-2.22)	2.76 (1.71-4.45)†
Immunosuppression‡	1.26 (0.62-2.59)	2.02 (1/13-3.61)†
Dementia	1.46 (0.91-2.37)	2.82 (1.61-4.97)†
Liver disease	3.88 (1.18-12.70)*	161 (0.39-6.67)
White blood cell count <4000/μL	2.99 (1.12-8.00)*	1.44 (0.50-4.18)
Serum urea nitrogen level >30 mg/dL (>10.7 mmol/L)	2.44 (1.62-3.68)*	1.15 (0.71-1.84)
Po_2 <60 mm Hg or oxygen saturation <90%	1.99 (1.32-3.00)*	1.33 (0.84-2.10)
Multilobar infiltrate	1.10 (0.74-1.63)	1.64 (1.07-2.49)†
Evidence of aspiration	3.09 (1.90-5.03)*	3.63 (2.05-6.45)†

*Significantly associated with pneumonia-related mortality.
†Significantly associated with pneumonia-unrelated mortality.
‡Defined as 1 or more of the following: use of an immunosuppressive agent within 90 days of presentation, a white blood cell count less than 3/μL, asplenia, hypogammaglobulinemia, use of systemic corticosteroids (prednisone, ≥10 mg/d, or its equivalent), and/or solid organ transplantation.

ity. However, our assumption that missing values were normal has been used in our prior validated models of pneumonia severity. Finally, the moderate number of deaths in this study may have limited the ability to detect clinical predictors of mortality and our ability to distinguish differences in the magnitude of effect for pneumonia-related and pneumonia-unrelated mortality.

In conclusion, this study demonstrates that there are significant differences between pneumonia-related and pneumonia-unrelated mortality, including the underlying and immediate causes of death, the timing of death, and the clinical predictors of death. These findings suggest that researchers, and those interested in evaluating the quality of pneumonia care, should use a strategy to differentiate between pneumonia-related and pneumonia-unrelated mortality. Possible strategies include using a shorter follow-up (≤30 days) or using a clinical review committee to assign the role of community-acquired pneumonia in the processes leading to death.

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