Pneumonia

Still the Old Man's Friend?

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Background: Hospital mortality of patients admitted with community-acquired pneumonia (CAP) has been well described. However, the long-term survival of those discharged alive is less clear. We sought to determine long-term survival of patients hospitalized with CAP and compare the outcome with controls hospitalized for reasons other than CAP.

Methods: We performed a matched case-control analysis using the Medicare hospital discharge database from the first quarter of 1997. We compared all Medicare recipients 65 years or older hospitalized with CAP and controls matched for age, sex, and race hospitalized for reasons other than CAP. We measured 1-year mortality determined from the Medicare Beneficiary Entitlement file and the Social Security Administration.

Results: We identified 158 960 CAP patients and 794 333 hospitalized controls. Hospital mortality rates for the CAP cohort and hospitalized controls were 11.0% and 5.5%, respectively ($P<.001$). One-year mortality rates for the CAP cohort and hospitalized controls were 40.9% and 29.1%, respectively ($P<.001$). One-year mortality rates in hospital survivors of the CAP and control cohorts were 33.6% and 24.9%, respectively ($P<.001$). The difference in mortality between the CAP and control cohorts was not explained by underlying disease. Standardized against the general population, the risk of death for both cohorts decreased monthly but was still elevated 1 year after hospital discharge. The standardized mortality ratio was 2.69 (95% confidence interval, 2.47-2.93) for CAP patients and 1.93 (95% confidence interval, 1.79-2.08) for hospital controls.

Conclusions: Almost half of all elderly patients admitted for CAP die in the subsequent year, with most deaths occurring after hospital discharge. The mortality is considerably higher than that of either the general population or a control population hospitalized for reasons other than CAP.

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SIR WILLIAM OSLER pointed out more than 100 years ago that pneumonia was a frequent, nonpainful, lethal event in elderly patients.[1] With advances in care, pneumonia no longer seems to portend such a poor prognosis. Many patients with community-acquired pneumonia (CAP) do not require hospitalization, and most who are admitted to the hospital survive to discharge. Nevertheless, CAP remains common and is still one of the leading causes of hospital admission and death throughout the world, including the United Kingdom[2] and United States.[3] Key risk factors seem to be advancing age and underlying disease.[4-16]

Less clear, however, is the subsequent fate of those who survive a hospitalization for CAP. Brancati et al[17] reported that 1 in 4 hospital survivors of CAP died in the following year. They found that underlying disease was the major risk factor for mortality, whereas age was not an independent predictor. They concluded that CAP was no longer "the old man's friend." However, this study and others[18,19] were of small sample size and often lacked control groups, potentially limiting their generalizability. Better information regarding the long-term outcome of patients surviving CAP would help in our understanding of this disease and aid clinical management and patient counseling.

We conducted a retrospective cohort study in the elderly US population to determine the 1-year all-cause mortality of patients hospitalized with CAP. We compared the outcomes of CAP patients with an age-, sex-, and race-matched cohort of control patients hospitalized for reasons other than CAP. We also compared survival in both the CAP and control cohorts to an age-, sex-, and race-matched general population.

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METHODS

DATA SOURCES

We analyzed data from the first quarter of the 1997 Medicare hospital discharge database (MedPAR, Health Care Financing Administration, Washington, DC). MedPAR contains records of all US hospital discharges at nonfederal hospitals for Medicare enrollees. For each discharge, we selected age, sex, race, admission, and discharge diagnosis codes (*International Classification of Diseases, Ninth Revision, Clinical Modification [ICD-9-CM]*),[20] length of stay, discharge status, and admission to day of death. We used US life tables to generate age-, sex-, and race-specific death rates.[21]

IDENTIFICATION OF STUDY COHORTS

CAP Cohort

We selected all patients 65 years or older who were hospitalized in acute care hospitals with a diagnosis of CAP. We defined CAP as either pneumonia (*ICD-9-CM* codes 481, 482, 485, or 486) listed as both the admission diagnosis and a discharge diagnosis or pneumonia listed as a discharge diagnosis coupled with a pulmonary complaint on admission (respiratory failure [518.81], chronic obstructive pulmonary disease [496], respiratory abnormality [786.09], complicated chronic obstructive pulmonary disease [491.21], food/vomit pneumonitis [507.0], acute bronchitis [466.0], asthma without status asthmaticus [493.90], hemoptysis [786.3], or other pulmonary insufficiencies [518.82]). Patients transferred from other hospitals were excluded because we were not able to differentiate CAP from nosocomial pneumonia (n=7300). However, we did not exclude nursing home residents from the analysis, a population included in the most recent official statement of the American Thoracic Society.[22]

Hospitalized Controls

For each patient hospitalized with CAP, we randomly selected 5 age-, sex-, and race-matched controls from the same MedPAR database who did not meet the *ICD-9-CM* codes–based criteria for CAP.

PATIENT CLASSIFICATION

We classified patients by demographic characteristics (age, sex, and race) and underlying illness according to the Charlson-Deyo comorbidity index (a measure of chronic illness derived from the presence of specific *ICD-9-CM* discharge diagnosis codes).[23]

MORTALITY ASSESSMENT

We determined hospital mortality from the MedPAR discharge status. We determined 1-year mortality from the admission to day-of-death field. Admission to day of death specifies the number of days from the beneficiary's hospital admission to the day of death and is entered into MedPAR based on data from the Medicare Beneficiary Entitlement file and the Social Security Administration. This field showed a high internal consistency with the length of stay for patients who died in the hospital (Kohen κ, 98.6; 95% confidence interval, 98.4-98.8). Because we did not have unique patient identifiers in the MedPAR data set, we were concerned about double counting deaths due to multiple admissions. Therefore, to explore this further, we conducted an analysis of the California hospital discharge data set,[24] which includes unique patient identifiers. Among Medicare patients with CAP in this data set, only 3.5% were readmitted to the hospital within 3 months of discharge. Therefore, the maximum rate of double-counted deaths was 0.035 per death.

STATISTICAL ANALYSIS

Our primary outcomes were time to death from hospital admission for all patients and time to death from hospital discharge for hospital survivors. We calculated postdischarge survival by subtracting length of stay from admission to day of death for hospital survivors. We generated monthly risks of death after hospital discharge for CAP patients and hospital controls from the number at risk at the beginning of each monthly interval and the number of deaths observed during this period. We determined standardized mortality ratios for the 1st, 3rd, 6th, and 12th months after hospital discharge by totaling the observed number of deaths for each month after hospital discharge and dividing by the expected number of deaths for the same period calculated from age-, sex-, and race-specific death rates using US life tables.[21] We reported baseline characteristics as proportions and compared them using Pearson χ^2 statistics. We determined independent predictors of hospital mortality by logistic regression. We computed survival estimates using the Kaplan-Meier product limit method.[25] We considered the death of individuals after the end of the follow-up period as censored observations. We performed a stratified direct adjustment for age, sex, race, and comorbid illnesses as appropriate.[26] We used Wilcoxon (Breslow) statistics to assess differences in survival. We assumed a significance level at $P<.001$ because of the large sample size. Data were managed using Visual FoxPro statistical software (Microsoft Corp, Redmond, Wash) and analyses conducted using Stata statistical software (Stata Corp, College Station, Tex).

RESULTS

BASELINE CHARACTERISTICS

CAP Cohort

We identified 161 164 elderly patients hospitalized with CAP. We excluded 2204 patients from analysis because of missing or corrupted data (**Figure 1**). Characteristics of the remaining 158 960 elderly patients are provided in **Table 1**. Pneumonia was diagnosed at both admission and discharge in 81% of the study cohort. Those who had a pulmonary complaint at admission and pneumonia recorded at discharge had similar baseline characteristics and outcomes to those who had pneumonia recorded at both admission and discharge (data not shown). More than 40% of the CAP cohort was 75 to 84 years old. There were slightly more women than men ($P<.001$). Almost 90% were white and 8% were African American. More than two thirds had an underlying disease, with chronic pulmonary disease and cardiovascular disease reported most commonly.

Hospitalized Controls

The hospitalized control cohort consisted of 794 333 age-, sex-, and race-matched, randomly selected Medicare recipients admitted to the hospital for reasons other than CAP. Characteristics of the control cohort are provided in Table 1. Hospitalized controls had lower rates

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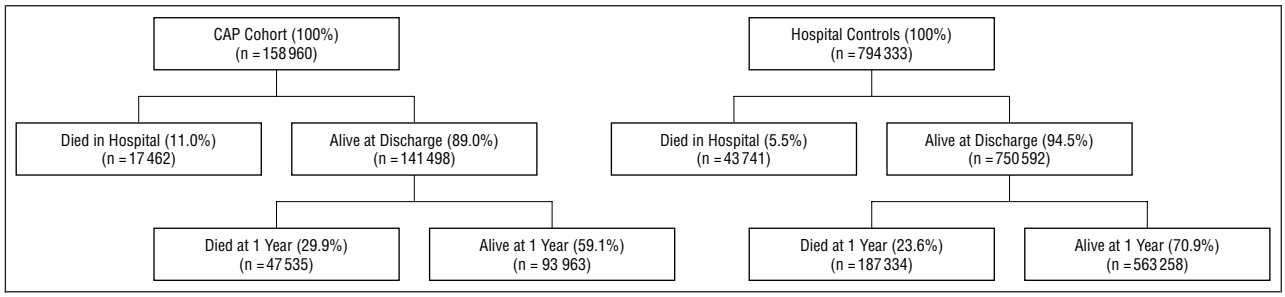

Figure 1. Identification and construction of the study cohorts. Patients were selected from the first quarter of the 1997 Medicare hospital discharge database and represent patients 65 years or older. Community-acquired pneumonia (CAP) was defined using *International Classification of Diseases, Ninth Revision, Clinical Modification* codes as either pneumonia listed as both the admission diagnosis and a discharge diagnosis or pneumonia listed as a discharge diagnosis coupled with a pulmonary complaint on admission. We generated a hospitalized control cohort by randomly selecting age-, sex-, and race-matched Medicare patients hospitalized for reasons other than CAP. We determined 1-year mortality from the Medicare Beneficiary Entitlement data file and the Social Security Administration. For both cohorts, we present hospital mortality and postdischarge mortality in separate frames, both of which total 1-year mortality.

than CAP patients of chronic pulmonary disease and chronic cardiovascular disease but higher rates of diabetes mellitus and malignancies. Other significant differences were small. Overall, 69.2% of the CAP patients and 63.4% of the hospitalized controls had one or more underlying illnesses.

HOSPITAL MORTALITY

CAP Cohort

One of 10 CAP patients died during hospitalization (**Table 2**). Hospital mortality increased with age and the number of comorbid illnesses. The highest hospital mortality was found in patients with renal disease, liver disease, and malignancy. Hospital mortality was higher for men and African Americans ($P<.001$). Using logistic regression, advanced age, increasing number of comorbidities, male sex, and black race were all independent predictors of hospital mortality ($P<.001$).

Hospitalized Controls

Hospital mortality for controls was half that for CAP patients, both overall and across most age-, sex-, race-, and comorbidity-specific subgroups (Table 2).

ONE-YEAR MORTALITY

CAP Cohort

One year after hospital admission, mortality for all CAP patients was more than 40% (Table 2). One-year mortality doubled with age from one third for patients 65 to 69 years old to almost two thirds for patients 90 years or older. One-year mortality increased with the number of comorbidities and was twice as high for patients with 3 or more comorbidities compared with patients with no comorbidity. One-year mortality rates of more than 50% were observed in CAP patients with metastatic solid tumors, other malignancies, renal disease, liver disease, and neuropsychiatric disorders (Table 2). After adjusting for age and comorbidity, mortality was higher in men (44.1% vs 35.3%, $P<.001$) and in the African American population (43.2% vs 39.0%, $P<.001$) (**Figure 2**).

Table 1. Baseline Characteristics for the Community-Acquired Pneumonia (CAP) Cohort and for an Age-, Sex-, and Race-Matched Hospitalized Control Cohort*

Characteristic	CAP Cohort (n = 158 960), %	Hospital Controls (n = 794 333), %	*P* Value
Age range, y			
65-69	14.4	14.4	.95
70-74	18.2	18.9	.93
75-79	20.5	20.5	.94
80-84	20.4	20.4	.97
85-89	15.3	15.3	.96
≥90	11.1	11.1	.79
Sex			
Male	46.8	46.8	.92
Female	53.2	53.2	.92
Race/origin			
Non-Hispanic white	89.5	89.5	.61
Non-Hispanic black	7.9	7.9	.99
Others	2.6	2.6	.32
Underlying disease†			
Cardiovascular	36.2	31.8	<.001
Pulmonary	25.0	12.0	<.001
Diabetes mellitus	17.0	19.2	<.001
Neuropsychiatric	8.7	9.2	<.001
Malignancy	8.1	10.3	<.001
Metastatic solid tumor	3.1	4.6	<.001
Renal	2.7	2.5	<.001
Hepatic	0.6	1.0	<.001
No. of comorbidities			
0	30.8	36.6	<.001
1	38.6	35.4	<.001
2	22.2	19.9	<.001
≥3	8.5	8.2	<.001

*The CAP cohort consisted of all beneficiaries 65 years or older hospitalized for CAP identified from the 1997 US Medicare hospital discharge database using *International Classification of Diseases, Ninth Revision, Clinical Modification* (*ICD-9-CM*) codes. The hospitalized control cohort consisted of age-, sex-, and race-matched patients hospitalized for reasons other than CAP selected randomly from the same data source.

†Underlying diseases were identified using the Charlson-Deyo comorbidity index based on the presence of specific *ICD-9-CM* discharge diagnosis codes.

Hospitalized Controls

One year after hospital admission, mortality was more than 10% lower in hospitalized controls than in CAP patients (Table 2). One-year mortality in control patients

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Table 2. Hospital and 1-Year Mortality for the Community-Acquired Pneumonia (CAP) Cohort and for an Age-, Sex-, and Race-Matched Hospitalized Control Cohort*

Characteristic	Hospital Mortality, %		1-Year Mortality, %†	
	CAP Cohort	Hospital Controls	CAP Cohort	Hospital Controls
All	11.0	5.5	40.9	29.1
Age range, y				
65-69	7.9	3.6	31.3	20.1
70-74	8.7	3.9	33.4	21.0
75-79	10.1	4.7	37.2	24.7
80-84	11.6	6.0	42.2	30.4
85-89	13.5	7.1	48.8	37.2
≥90	15.8	9.1	57.0	47.0
Sex				
Male	11.9	6.0	44.8	31.5
Female	10.2	5.0	36.9	26.6
Race/origin				
Non-Hispanic white	10.9	5.4	40.4	28.6
Non-Hispanic black	11.7	6.2	43.1	32.6
Others	10.8	5.6	40.7	28.4
Comorbidities				
Cardiovascular	14.2	8.6	48.6	38.0
Neuropsychiatric	12.3	5.9	52.7	39.8
Pulmonary	10.5	7.3	41.7	37.8
Hepatic	21.6	13.6	56.2	54.0
Diabetes mellitus	10.3	5.1	39.8	30.0
Renal	24.4	13.9	64.7	56.5
Metastatic solid tumor	23.4	11.9	85.5	71.2
Other malignancy	17.7	8.5	69.7	52.1
No. of comorbidities				
0	7.8	2.9	29.4	16.2
1	10.7	5.5	40.1	29.7
2	13.9	8.2	50.4	41.9
≥3	16.2	10.5	57.4	49.3

*The CAP cohort consisted of all beneficiaries 65 years or older hospitalized with CAP identified from the first quarter of the 1997 US Medicare hospital discharge database using *International Classification of Diseases, Ninth Revision, Clinical Modification* codes. The hospitalized controls were an age-, sex-, and race-matched cohort hospitalized for a reason other than CAP selected randomly from the same data source.

†We used Wilcoxon (Breslow) statistics to assess differences in 1-year survival. *P* values were significant for all comparisons (<.001).

increased with age and the number of comorbid illnesses similar to that of CAP patients, but an absolute mortality difference of more than 10% was observed across most age-, sex-, race-, and comorbidity-specific subgroups (Table 2). The differences in 1-year mortality for CAP patients and hospitalized controls persisted after adjusting for comorbidity (40.4% vs 29.2%, $P<.001$) (**Figure 3**).

POSTDISCHARGE MORTALITY

Mortality rates for the 1st, 3rd, 6th, and 12th months after hospital discharge for hospital survivors of the CAP and control cohorts are provided in **Table 3**. Within 12 months of hospital discharge, 1 of 3 survivors of hospitalized CAP and 1 of 4 hospital survivors of the control cohort died. After adjusting for comorbidity, 1-year postdischarge mortality rates for CAP patients and controls were 33.6% and 24.9%, respectively ($P<.001$) (Figure 3). The risk of death decreased during each consecutive month after hospital discharge (Table 3). However, at 12 months after hospital discharge, the risk of death for CAP patients and hospitalized controls remained elevated compared with that of an age-, sex-, and race-matched general US population and was higher for CAP patients than for controls.

COMMENT

We determined 1-year outcome in more than 150 000 elderly Medicare recipients hospitalized with CAP. One-year all-cause mortality was 4 times higher than hospital mortality. One of 3 elderly patients who survived hospitalization for CAP died in the year following hospital discharge. Although a substantial proportion of deaths occurred in the first 3 months following discharge, the increased risk of death persisted for the entire year of follow-up. The magnitude and duration of this effect were not explained by need for hospital admission or comorbidity. To our knowledge, this is the first study to describe long-term survival following hospital admission for CAP on a national level. Our data confirm Osler's notion and show that even today, with many preventive and therapeutic measures, there is a high risk of death during the next few months in elderly patients discharged from the hospital after an episode of CAP.

Our study confirmed a substantial long-term mortality in survivors of CAP as reported in earlier, smaller studies.[17-19] One study of 141 adult CAP patients of all age groups reported a 1-year postdischarge mortality rate of 25%.[17] Hedlund et al[18] found a 2.5-year postdischarge mortality rate of 21% in 241 patients 18 years or older hospitalized with CAP. A Finnish population-based study followed up 122 elderly patients who survived hospitalization for CAP for up to 9 years.[19] Mortality was 19% at 1 year, 32% at 2 years, and 54% at 5 years, and the risk of death remained elevated for the entire follow-up period compared with other elderly inhabitants from the same region.

Our results show that advanced age and increasing number of comorbidities were major independent predictors of 1-year mortality. Contrasting these results and other reports,[18,19] Brancati et al[17] found that after adjusting for comorbidities, age was not an independent predictor of mortality. A possible explanation for this discrepancy might be the exclusion of nursing home residents, an elderly group likely to die, from the study by Brancati and coauthors.

An advantage of our study is the ability to compare long-term outcome of hospitalized CAP with that of age-, sex-, and race-matched controls hospitalized for reasons other than CAP, evaluating the independent association of CAP with long-term mortality. We believe that considering mortality with and without adjustment for comorbidities is important, since CAP might merely be a marker of underlying illness and not in itself a predictor of poor outcome. However, although 1-year mortality was high in all hospitalized patients, the pneumonia cohort had higher comorbidity-adjusted 1-year mortality than the control cohort, suggesting that CAP's effects on mortality may be independent of the need for hospitalization or underlying disease. Therefore, CAP is either a disease with some unknown long-term sequelae

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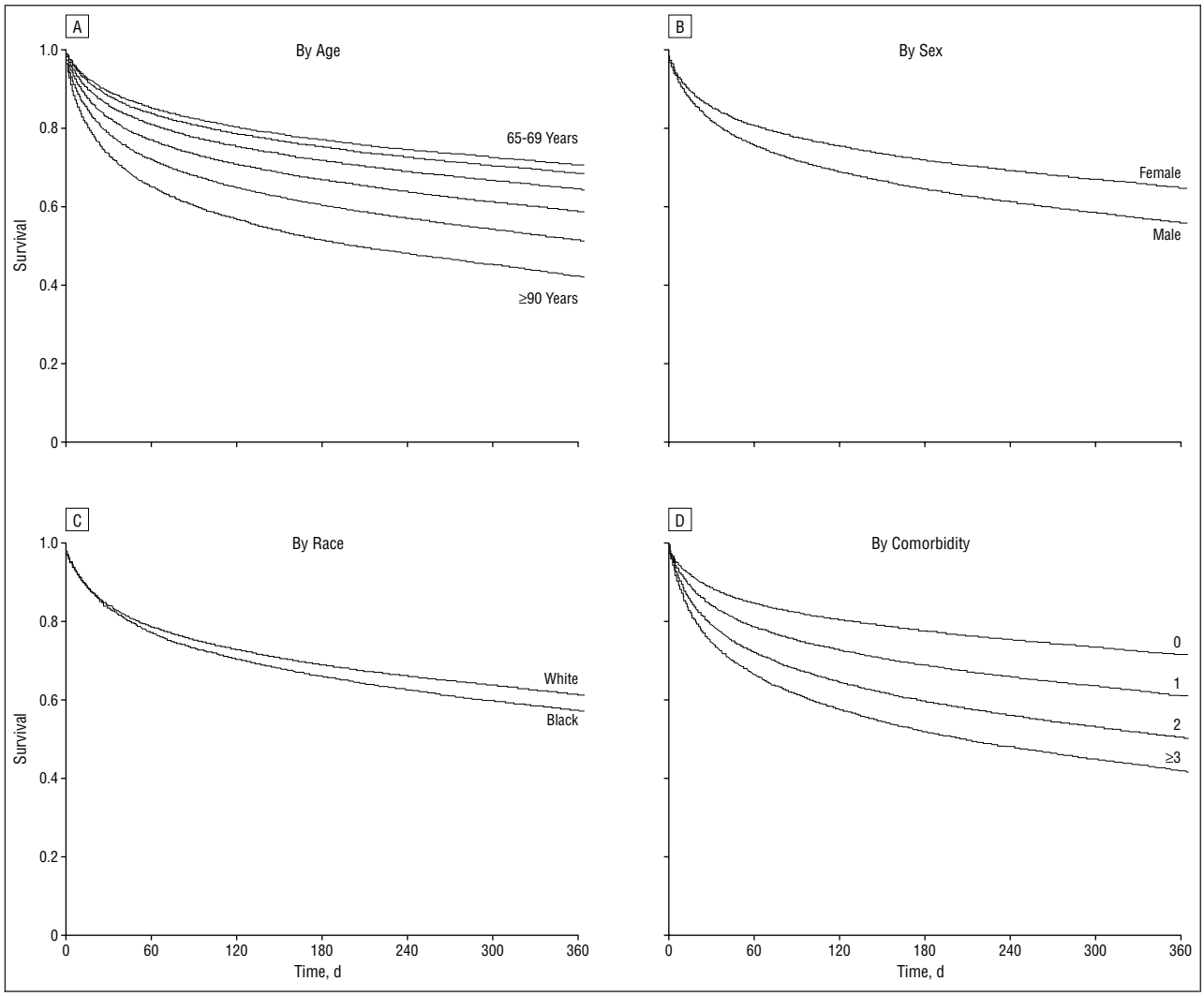

Figure 2. Adjusted Kaplan-Meier survival estimates for the community-acquired pneumonia cohort stratified by age (A), sex (B), race (C), and comorbidity (D). Age-stratified survival estimates are presented for patients aged 65 through 69 years, 70 through 74 years, 75 through 79 years, 80 through 84 years, 85 through 89 years, and 90 years or older (top to bottom). We defined comorbidities using Charlson-Deyo comorbidity index. Stratified survival curves for comorbidities were based on the number of underlying illnesses. We adjusted survival curves using a stratified direct adjustment. We used Wilcoxon (Breslow) statistics for stratified analysis to assess differences in survival. Older age, male sex, black race, and number of comorbid illnesses were associated with increased mortality ($P<.001$ for all comparisons).

that affect survival beyond the acute episode or a nonrandom disease that strikes a population that is at higher risk of death compared with the general population. Indeed, pneumonia itself might be a more sensitive marker of comorbidities with unfavorable prognosis than commonly used measures based on patient records.

There are important implications from this study. First, long-term survival needs consideration in all CAP patients. It is critical for a patient's prognostication and for family counseling, and it may have important implications for medical decision making, such as whether to continue life support and aggressive medical care. Second, hospital mortality is not an appropriate outcome measure for studies in elderly patients with CAP, since beneficial or detrimental aspects of interventions may not manifest within this time frame. Third, future efforts in the treatment of patients with CAP have to consider the postdischarge period, where most deaths occur. Interventions, such as pneumococcal and influenza vaccination,[19] and nonspecific measures, such as regular physical activity and better social support, may improve postdischarge outcome.

Our study was based on administrative data. Such data provide insight into the large-scale effects of disease on the health of a population but lack the level of clinical detail found in prospective clinical data sets. The general limitations of administrative data for research have been well described.[27-31] There are also specific caveats to this study. Previous CAP studies using administrative data selected all patients with a principal discharge diagnosis of pneumonia. To avoid missing patients with pneumonia, we included a pneumonia diagnosis recorded in any discharge field. However, to minimize inclusion of patients with hospital-acquired pneumonia, we also required a diagnosis of pneumonia or a pulmonary complaint at admission. The extent to which this scheme improved the accuracy of diagnosis of CAP is unknown. We may have double counted some deaths in the CAP

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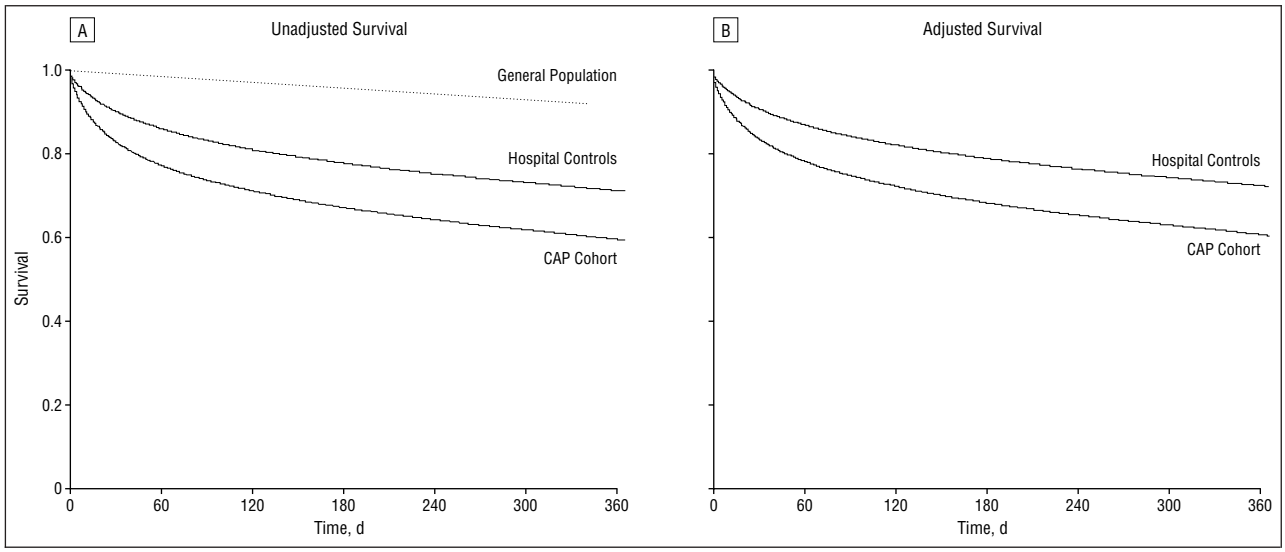

Figure 3. Unadjusted and comorbidity-adjusted Kaplan-Meier survival estimates for age-, sex-, and race-matched cohorts of elderly patients hospitalized with community-acquired pneumonia (CAP) and for reasons other than CAP. Comorbidities were defined using the Charlson-Deyo comorbidity index. Unadjusted (A) and comorbidity-adjusted (B) survival estimates are presented for CAP patients and hospitalized controls. Expected survival in an age-, sex-, and race-matched US population is presented as a dotted line and was generated from US life tables. Unadjusted and comorbidity-adjusted 1-year mortality was higher for CAP patients than for hospitalized controls ($P<.001$).

Table 3. Mortality, Monthly Risk of Death, and Standardized Mortality Ratios (SMRs) for the 1st, 3rd, 6th, and 12th Months After Hospital Discharge for Community-Acquired Pneumonia (CAP) Patients and Controls*

Period and Cohort	Mortality, % (95% CI)	Risk of Death, % (95% CI)	SMR (95% CI)
First month after discharge			
CAP patients	9.4 (9.3-9.6)	9.43 (9.28-9.59)	13.2 (12.3-14.3)
Controls	6.1 (6.0-6.2)	6.09 (6.03-6.14)	8.54 (7.93-9.19)
Third month after discharge			
CAP patients	18.0 (17.9-18.2)	4.13 (4.02-4.25)	5.77 (5.34-6.24)
Controls	12.5 (12.4-12.6)	3.01 (2.97-3.05)	4.22 (3.92-4.55)
Sixth month after discharge			
CAP patients	25.0 (24.9-25.2)	2.54 (2.46-2.64)	3.56 (3.28-3.86)
Controls	18.0 (17.9-18.1)	1.84 (1.80-1.87)	2.58 (2.39-2.78)
Twelfth month after discharge			
CAP patients	33.6 (33.5-33.8)	1.92 (1.81-1.99)	2.69 (2.47-2.93)
Controls	24.9 (24.8-25.0)	1.37 (1.35-1.41)	1.93 (1.79-2.08)

Abbreviation: CI, confidence interval.

*The SMRs were calculated from age-, sex-, and race-specific death rates per 100 000 population determined from US life tables.[21] The CAP patients consisted of all Medicare survivors 65 years or older hospitalized for CAP and discharged from the hospital in the first quarter of 1997. The controls were age-, sex-, and race-matched survivors of hospitalizations for reasons other than CAP selected randomly from the same data source.

and control cohorts because of a lack of unique patient identifiers. However, by additional analysis, we estimate that double counting could have inflated mortality rates by a maximum of 1.1% at 12 months and by much smaller amounts at 1 (0.3%), 3 (0.6%), and 6 (0.8%) months. We do not believe that this double counting significantly affected any of our analyses or conclusions. Our results are also limited to patients with CAP who required hospitalization and do not include individuals treated as outpatients.

In conclusion, hospitalized CAP is associated with many deaths outside the time frame normally considered in this otherwise acute disease. As clinicians, we need to consider the effects of CAP on mortality far beyond hospital discharge. The observed high mortality rates are important for prognostication, patient and family counseling, and medical decision making. Improved understanding of the poor long-term prognosis associated with CAP is needed to modify the dismal outcome of this common disease in elderly patients.

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