Prognosis After Community-Acquired Pneumonia in the Elderly

A Population-Based 12-Year Follow-up Study

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Background: Only a few studies have investigated the long-term effects of community-acquired pneumonia (CAP). These studies have focused on cases treated in the hospital, and, to our knowledge, no long-term survival studies that include all cases of CAP are available.

Methods: A prospective observational study on the survival rates in a population-based cohort of elderly inhabitants aged 60 years or older at baseline in 1 township in eastern Finland in 1983. A total of 4167 (99% of the total elderly population), 122 of whom survived CAP during a prospective pneumonia surveillance period from 1983 to 1985, were followed up for mortality from 1983 to 1994 for a median of 9.2 years. The relative risk (RR) of death in patients who survived CAP was compared with that in elderly inhabitants without CAP by Cox multivariate regression analysis. Data on causes of death were obtained from a central register based on death certificates.

Results: The long-term survival rate was significantly lower in persons who had survived CAP or pneumococcal CAP (PCAP) than in the rest of the study population. The RR of pneumonia-related mortality was 2.1 (95% confidence interval [CI], 1.3-3.4; P = .004) in all patients with CAP and 2.8 (95% CI, 1.5-5.3; P = .001) in patients with PCAP. The respective numbers for total mortality were 1.5 (95% CI, 1.2-1.9; P = .001) in all patients with CAP and 1.6 (95% CI, 1.1-2.2; P = .01) in those with PCAP. Also the risk of cardiovascular mortality was increased in persons with CAP (RR, 1.4; 95% CI, 1.0-1.9; P = .02) and in those with PCAP (RR, 1.6; 95% CI, 1.0-2.4; P = .04).

Conclusions: The present results indicate that elderly patients treated for CAP are at high risk of subsequent mortality for several years. Based on the high incidence and negative long-term effects of pneumonia, it can be concluded that there is a clear need for prevention, eg, by influenza and pneumococcal immunization.

Arch Intern Med. 1999;159:1550-1555

COMMUNITY-acquired pneumonia (CAP) is an increasing problem among the elderly. In the United States, approximately 1 600 000 persons were discharged from short-stay hospitals after treatment for pneumonia based on first- and second-listed diagnoses in 1990; elderly persons aged 65 years or older accounted for 52% of all pneumonia discharges. According to a survey of the national hospital discharge register in Finland, annual hospital treatment periods for all pneumonia cases increased between 1972 and 1993 from 15.5 to 23.9 per 1000 population aged 65 years or over. The high incidence of pneumonia in young children and elderly people has been a general feature in previous studies; however, detailed data on the incidence of pneumonia in the population with age- and gender-specific figures are rare; in industrialized countries, the annual incidence of CAP in persons aged 13 to 15 years or older has varied from 2.6 to 9.0 per 1000 persons. Several studies indicate that age and underlying diseases are the most important risk factors for contracting pneumonia, and elderly persons with high-risk conditions have excess hospitalization and death rates as a result of pneumonia. However, most of this information is based on hospitalized patients or other selected patient groups, and prospective, population-based studies are rare. Despite the importance of pneumonia as an immediate cause of illness and death, only a few studies have investigated the long-term effects of CAP. Furthermore, such studies have focused on cases that have been treated in the hospital and, to our knowledge, no long-term survival studies that include information on all cases of CAP are available.

We have previously reported on the risk factors for and the incidence of CAP as well as on the efficacy of the pneumococcal vaccine in the entire elderly population of the township of Varkaus in eastern Finland. A follow-up of this population made it possible to compare long-term outcome in patients who survived CAP with that in all other elderly inhabitants who did not get pneumonia.
PATIENTS AND METHODS

All elderly (≥60 years of age) inhabitants (N = 4213) of a small town in eastern Finland were followed up for pneumonia from January 1, 1983, to December 31, 1985, in a previously reported, randomized pneumococcal vaccination trial and a connected study on the risk factors for contracting pneumonia. The study population in the present analysis included 4167 persons (99% of the total elderly population) for whom the pneumococcal vaccination status was registered in 1982 (1364 persons received both pneumococcal and influenza vaccines; 1473 persons received influenza vaccine alone; and 1330 were registered as nonrespondents). During the 3-year follow-up period (1983 to 1985), a total of 271 cases of suspected pneumonia were registered in the study population, including both community-acquired and nosocomial cases; 205 cases in 185 patients fulfilled the criteria for pneumonia (ie, the presence of an acute radiographic infiltrate and coexistent symptoms or signs indicative of a lower respiratory tract infection [186 episodes] or the presence of an acute, radiographically typical case of pneumonia registered by the attending physician even if the clinical criteria were not fulfilled [19 episodes]). Pneumococcal pneumonia was serologically diagnosed as reported previously in 83 cases, corresponding to 40% of all cases of pneumonia and to an incidence of 7.0 per 1000 person-years. The number of all cases of CAP was 145 (71%), corresponding to an incidence of 12.3 per 1000 person-years; of these, 57 (39%) were treated at home and 88 (61%) were treated in the hospital or in a health center ward. The number of hospital- or institution-acquired pneumonias was 60. Streptococcus pneumoniae was the causative agent in 63 episodes of CAP occurring in 57 patients (43% of all community-acquired cases), corresponding to an incidence of 5.3 per 1000 person-years. The enrollment of study participants, collection of baseline data, and the incidence of pneumonia have been reported previously. There were 122 patients (84%) who survived radiologically diagnosed CAP (ie, period of treatment less than 60 days from the date of the first pneumonia episode to the date of death); of these, 69 (57%) required treatment in the hospital and 53 (43%) received a diagnosis of pneumococcal pneumonia. Data on causes of death during the period from 1983 to 1994 were obtained from a central register based on death certificates using International Classification of Diseases, Eighth Revision (ICD-8) and International Classification of Diseases, Ninth Revision (ICD-9) codes. The coverage of this register in Finland is 100%; thus, mortality could also be ascertained for persons who left the region. The patients with pneumonia were identified during the prospective pneumonia surveillance period from 1983 to 1985, and the survival curves were drawn for the years from 1983 to 1994. The long-term survival of the 122 patients who survived CAP was compared with the survival of all other inhabitants who did not get pneumonia (n = 4045) by analysis of the differences in pneumonia-related mortality (pneumonia as the immediate, intermediate, underlying, or contributing cause of death, ICD-8 codes 48090 to 48690 and ICD-9 codes 4800 to 4859), in total mortality, and in cardiovascular mortality (ICD-8 codes 39007-45890 and ICD-9 codes 3900-4599). In the present study, subsequent pneumonia-related deaths were recorded without specification of an etiologic agent, and we relied on the treating physicians with regard to the diagnosis of pneumonia; the accuracy of reporting was not assessed.

Baseline data on chronic conditions in the study population were obtained in September 1982 from a computer-based register managed by the municipal health center of Varkaus, Finland, which covers all inhabitants and includes complete records of both outpatient and hospital diagnoses determined by a physician. One of us (M.S.) reviewed this database for the presence of predefined chronic conditions, with special attention to potential medical risk factors for pneumonia. Comorbidities present at baseline and pneumococcal vaccination status were included in the risk analysis. The following conditions were tested (ICD-8 codes): hypertension (400-404) (only hypertension requiring medication was considered); heart disease (393-398; 426.01-426.09; 427.00), including aortic, mitral, or pulmonary stenosis, cor pulmonale, congenital heart disease with pulmonary hypertension, chronic compensated heart failure with medication (96% of heart disease), and chronic congestive heart failure (1.6% of heart disease); other cardiovascular disease (410-414; 427.20-427.98; 440.00-440.99), including coronary artery disease or arrhythmia without heart failure and oblitative arteriosclerosis; all types of diabetes (250), including those treated with diet alone; chronic pyelonephritis (590.0), including renal parenchymal disease diagnosed radiologically, by biopsy, or by functional tests; lung disease (491.01-492.09; 517.01-517.09; 519.00-519.28; 010-019; 518.99; 160-163), including chronic bronchitis, pulmonary embolism, chronic interstitial lung disease, sequelae of tuberculosis, bronchiectases, and lung cancer; bronchial asthma (493.00-493.09) (only asthma requiring medication was considered); connective tissue disease (712.00-712.50; 716.00-716.10; 734.00-734.99), including rheumatoid arthritis; cancer (140-199; 200-209) (only malignancies diagnosed during the last 5 years were included); thyroid dysfunction (242.00-242.20; 243.9; 244.0-244.9), including hyperthyroidism and hypothyroidism; immunosuppressive therapy, including treatment with cytostatics, radiation, or corticosteroids currently or within 1 year; alcoholism (303.0-303.9); and institutionalization (resident in hospital or home for the elderly).

The Cox multivariate regression model was used to assess the relative risk (RR) of subsequent death in persons who survived CAP compared with those without pneumonia; variables that were significantly associated with mortality in univariate analysis (P < .05) were included in the multivariate analysis. For drawing the survival curves, the actuarial table-method was used to evaluate the cumulative proportion of survivors at each year of follow-up. All statistical procedures were performed with a commercially available software program (SPSS Inc, Chicago, Ill; IBM RS6000/590 Aix, University of Kuopio, Kuopio, Finland).

The study was approved by the health authorities of Varkaus and the Ethics Review Committee of the National Public Health Institute, Helsinki, Finland, and the Ministry of Social Affairs and Health approved the use of the death certificate register.
The 4167 study subjects were followed up from January 1, 1983, to December 31, 1994, for a median of 9.2 years (total number of person-years, 38,170). During that time, a total of 1979 deaths from all causes were registered from the death certificates. In 61% of cases, the cause of death was cardiovascular. The total number of deaths from pneumonia was 331, representing 16.7% of deaths from all causes. Pneumonia was registered as the immediate, intermediate, underlying, or contributing cause of death in 208, 4, 95, and 24 cases, respectively. The overall pneumonia-related mortality rate was 8.7 per 1000 person-years.

Of the 122 elderly patients who survived CAP during the prospective pneumonia-surveillance period from 1983 to 1985, 109 (89%) were alive after 1 year of follow-up, 97 (80%) after 2 years, 73 (60%) after 5 years, and 48 (39%) after 10 years; the respective numbers for the 69 patients treated in the hospital for CAP were 56 (81%) after 1 year, 47 (68%) after 2 years, and 32 (46%) after 5 years, and 18 (26%) after 10 years. Of the 4045 persons without CAP, 96% were alive after 1 year of follow-up, 92% after 2 years of follow-up, 81% after 5 years of follow-up, and 61% after 10 years of follow-up.

Figure 1 and Figure 2 illustrate that CAP and pneumococcal CAP (PCAP) were significantly associated with decreased subsequent long-term survival, the effect lasting throughout the whole follow-up period. The RR of pneumonia-related mortality was 2.1 (95% confidence interval [CI], 1.3-3.4; \( P = .004 \)) in all patients with CAP and 2.8 (95% CI, 1.5-5.3; \( P = .001 \)) in those with PCAP. The respective numbers for total mortality were 1.5 (95% CI, 1.2-1.9; \( P = .001 \)) in all patients with CAP and 1.6 (95% CI, 1.0-2.4; \( P = .04 \)) in those with PCAP. Also subsequent cardiovascular mortality was increased in patients with CAP (RR, 1.4; 95% CI, 1.0-1.9; \( P = .02 \)) or PCAP (RR, 1.6; 95% CI, 1.0-2.4; \( P = .04 \)).

Because common chronic conditions increase the risk of pneumonia-related mortality, and prognosis may largely
be related to comorbidity, 13 predefined conditions present at baseline were included in the risk-analysis, and several of them independently predicted mortality over the long-term follow-up. The Table shows multivariate analyses only for variables that were significantly (P < .05) associated with mortality in univariate analyses. We also did a multivariate analysis for pneumonia-related mortality, including pneumococcal vaccination status and all chronic conditions together in the model, whether or not they were significantly associated with mortality in the univariate analysis; the results were the same: variables with a nonsignificant association remained as such, and the relative risks for significant associations remained the same except for immunosuppressive therapy, which in this analysis tested not significant (RR, 3.2; 95% CI, 0.9-10.6; P = .06).

We also did subgroup analyses comparing patients with CAP who were treated in the hospital with those without CAP, as well as patients with CAP who were treated at home with those without CAP. The RRs were as follows for the cases of CAP treated in the hospital (n = 69): 3.4 (95% CI, 1.8-6.5; P < .001) for pneumonia-related mortality, 2.5 (95% CI, 1.9-3.3; P < .001) for total mortality, and 2.4 (95% CI, 1.7-3.4; P < .001) for cardiovascular mortality. When only those patients with CAP who were treated at home (n = 53) were compared with persons without CAP, the RR for pneumonia-related mortality was 2.3 (95% CI, 1.1-4.9; P = .03).

**COMMENT**

During a mean follow-up period of 9.2 years, we compared outcomes in elderly patients who had survived CAP with outcomes of other elderly inhabitants in the study area. We studied all patients with CAP, not only those requiring in-hospital treatment. The present results indicate that patients who are treated for pneumonia are at high risk of subsequent mortality for several years. Because it is well known that several chronic medical conditions increase the risk for pneumonia and pneumonia-related mortality, we included comorbidities present at baseline as well as the pneumococcal vaccination status in the present risk analysis. The subsequent pneumonia-related mortality in patients who survived CAP (in 57% of cases treated in the hospital) was twice as high as in other elderly inhabitants. If the pneumonia episode was caused by *Streptococcus pneumoniae*, the risk was 3 times higher. Subsequent total and cardiovascular mortality rates were also increased in persons who survived CAP.

**COMPARISON WITH OTHER STUDIES**

Based on a central register of death certificates, the overall pneumonia-related mortality rate (also including deaths in the acute phase) among the elderly was found to be higher than in some earlier studies—8.7 per 1000 person-years compared with 2.5 to 5.9 per 1000 elderly persons—and to account for a substantial proportion of total mortality (16.7%). Salive et al. reported the results from 6 years of follow-up among 10,269 persons aged 65 years or older in 3 communities in the United States: the pneumonia-related mortality rate was 4.3 per 1000 person-years in men and 1.4 in women using the underlying cause of death only. However, when all deaths with pneumonia were grouped together, the pneumonia-related mortality rate was 7.3 per 1000 person-years, representing 11% of all deaths. This figure is comparable to ours, because we also grouped all reported deaths with pneumonia together, whether it was an underlying, immediate, or contributing cause of death. The proportional
pneumonia-related mortality rates by age and sex found in our study (detailed data not shown) were also very similar to the rates found in a 10-year autopsy-based Japanese study.28

Long-term outcome studies on CAP are limited, since there are only a few studies in which patients have been followed up for even 1 year. Zweig et al21 found that 76% of the 99 elderly patients (older than 60 years) surviving after hospitalization for community-or nursing home-acquired pneumonia were alive after 1 year. Fedson et al29 found that 61% of 400 patients aged 65 years or older who survived hospital treatment for pneumonia during a 3-month influenza outbreak in Manitoba in 1982-1983 were alive after 5 years; the respective number for controls was 73%. In another study, 68% of the 119 patients aged 18 to 92 years who survived hospital treatment for CAP were still alive after 1 year; mortality was related to severe or moderate comorbidity but not to age.23

In long-term care facilities, 40% to 67% of the patients were found to be alive at 1 year after pneumonia, and 25% to 52% 2 years after pneumonia, depending on the Activities of Daily Living score.30 In the present study, 81% of the patients who were treated for CAP in the hospital were alive after 1 year; the 2-year figure (68% alive) was similar to that found previously,23 although all our patients were 60 years of age or older at baseline.

Hedlund et al31 studied factors of importance for the long-term prognosis after hospital treatment for CAP, and found that the risk of death from any cause was 2 times higher (RR 2.0; 95% CI, 1.4-3.2) in the patient population compared with the general population. Our result was almost the same (RR 1.9; 95% CI, 1.4-2.5). Previous hospital care, for any reason, has been proposed as an identification for persons at greater risk for acquiring pneumonia; the rate of pneumonia among persons aged 65 years or older discharged from hospital was 3% to 9% during the subsequent 5 years.32 In a retrospective study in Sweden, persons who previously received in-hospital treatment for pneumonia were found to have a more-than-5-times-higher risk of recurrent pneumonia and also higher subsequent mortality rates than controls.32 The results were confirmed in a recent prospective study during approximately 3 years of follow-up: the observed incidence of pneumonia was as high as 98 per 1000 person-years in middle-aged and elderly persons previously treated in hospital for CAP.4 It was almost 5 times higher than the overall incidence of pneumonia in persons older than 60 years in Finland.10 These results are in agreement with the present findings that patients with pneumonia have a 2- to 3-times-higher subsequent risk for pneumonia-related death over a mean of 9.2 years of follow-up. Also, in a recent Swedish pneumococcal vaccination trial33 the incidence of pneumonia and pneumococcal pneumonia was found to be high among patients aged 50 to 85 years who had been previously treated for CAP as inpatients. The incidence of pneumonia per 1000 persons was 40, 54, and 116 in 3 age groups: 50 to 65 years, 66 to 75 years, and 76 to 85 years, respectively.

We found that several common chronic conditions that were present before the pneumonia episode were independent risk factors for death from any cause and for death from pneumonia. Still, CAP was an independent risk factor for mortality. There are most likely other factors, not measured in this study, that contribute to prognosis, eg, social and behavioral factors, as well as functional status. In contrast to our findings, none of the chronic conditions studied by Hedlund et al31 were independent risk factors for death from pneumonia, and only non-lung malignancies and corticosteroid therapy were risk factors for death from any cause. Hedlund and colleagues retrospectively studied which factors that were present during hospital treatment for CAP were of importance for the long-term prognosis after discharge (average length of follow-up, 2 years 7 months). The following chronic conditions were studied: alcoholism, chronic obstructive pulmonary disease, other chronic pulmonary diseases, congestive heart failure, diabetes, cirrhosis of the liver, splenectomy, lung cancer, non–lung malignancies, and corticosteroid and cystotatic treatment. Hedlund and coworkers studied all patients aged 18 years or older; therefore, chronic conditions were present in only a few patients, causing a risk of false-negative results.31 In contrast, our patient population was 60 years of age or older, with 74% having at least 1 of the chronic conditions and 55% having independent risk factors for pneumonia.34

In the present study, we could not demonstrate reduction in overall pneumonia-related mortality or in total mortality resulting from pneumococcal vaccine; the results remained the same in a subgroup analysis among persons with risk factors for contracting pneumonia, as well as in an interim analysis for the first 6 years (data not shown). This observation may not reflect the inefficiency of the vaccine, because based on the present study design using a register of death certificates as the data source, all pneumonia-related deaths, not only those due to pneumococcal pneumonia, were considered, and “pneumonia deaths” in terminally ill patients are unlikely to be prevented.

**PRACTICAL SIGNIFICANCE OF THE RESULTS**

Since *S pneumoniae* is the most common etiologic agent for CAP, pneumococcal immunization at discharge has been suggested as a cost-effective prevention measure if the vaccine is effective.22,34,35 The present study showed that the risk for subsequent pneumonia-related long-term mortality in patients with CAP was more than 2 times greater than in non-CAP persons. The risk was increased in all patients with CAP, not only in those treated in the hospital. However, we think that it is important to analyze all cases of CAP together, because local patterns of admitting patients largely contribute to the hospitalization rate. Thus, there is a wide geographic variation in the incidence of pneumonia treated in the hospital, which reflects the incidence of severe cases only partially. In Finland, a large number of patients with pneumonia (70% of those aged 60 years or older) are referred to the hospital.10 Hospital-based pneumococcal immunization that is capable of reaching the patients who are most likely to develop pneumococcal disease has been proposed,36 but, to our knowledge, there are no prospective studies that have demonstrated the effectiveness of pneumococcal vaccination in patients with CAP. In fact, a recent Swedish trial showed no benefit from the 23-valent vaccine in preventing pneumococcal pneumonia among patients aged 50 to 85 years who had been previously treated for CAP as in-
patients.\textsuperscript{33} In contrast, we found pneumococcal vaccine to be 59\% effective in a subgroup of elderly persons with increased risk for pneumonia in a prospective, randomized pneumococcal vaccination trial,\textsuperscript{23} and there is convincing evidence of the efficacy of the pneumococcal vaccine against bacteremic infection.\textsuperscript{36-40} Also, influenza vaccine has been proved effective in preventing hospitalization for influenza and pneumonia and deaths from influenza-associated respiratory conditions among the elderly.\textsuperscript{41,42} In addition, if immunogenicity studies using conjugate vaccines under development\textsuperscript{43} also prove to be promising among the elderly, efficacy trials of such vaccines in pre-pneumococcal vaccination trials,\textsuperscript{25} and there is convincing evidence against bacteremic infection.\textsuperscript{36-40} Also, influenza vaccine of the work.

ods, and Camilla Jokinen, MD, for her advice during all stages Pirjo Halonen, MSc, for her advice with the statistical methods and critical reading of the manuscript, and the Orion Corporation Research Foundation. The present study provides new data on the long-term effectiveness of prevention programs is being estimated, and efforts should be taken to prevent the first episode of pneumonia.

Accepted for publication December 17, 1998.

This study was supported in part by the Paulo Foundation, the Päiviä and Sahari Sohberg Foundation, the Tampere Tuberculosis Foundation, the Väinö and Laina Kivi Foundation, and the Orion Corporation Research Foundation.

We thank Markku Laakso, MD, for his advice with the statistical methods and critical reading of the manuscript, Pirjo Halonen, MSc, for her advice with the statistical methods, and Camilla Jokinen, MD, for her advice during all stages of the work.

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