Original articles

Factors of importance for the long term prognosis after hospital treated pneumonia

Jonas U Hedlund, Åke B Örtqvist, Mats E Kalin, Fredrik Granath

Abstract

***Background*—Elderly patients admitted to hospital for community acquired pneumonia have a high risk of recurrence of pneumonia and of death during the years after discharge. In this study potential factors of importance for the long term prognosis after hospital treated pneumonia were retrospectively investigated.**

***Methods*—A total of 241 patients (103 men) with a mean age of 60 (range 18–102) years discharged from hospital after treatment for community acquired pneumonia were studied. After an average follow up period of 31 months, 18 independent variables present during hospital treatment of the initial pneumonia were examined for association with the following end points: recurrence of pneumonia, death from any cause, and death from pneumonia.**

***Results*—Age adjusted analysis showed that systemic treatment with corticosteroids correlated significantly with recurrence of pneumonia and with death. The presence of low serum albumin levels on admission or colonisation of the respiratory tract with Gram negative enteric bacteria seemed to be important negative prognostic factors for the outcome during pneumonia recurrences after discharge.**

***Conclusions*—Patients who are admitted to hospital with pneumonia are at risk of subsequent pneumonia and death after discharge. This risk seems to be even higher in patients who are treated with corticosteroids systemically, who have a low serum albumin level on admission, or who become colonised in the respiratory tract with Gram negative enteric bacteria during their hospital stay.**

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Pneumonia continues to be a major cause of morbidity and mortality even in highly developed countries. In Sweden pneumonia accounts for more than 5% of all deaths and is the third leading cause of death after vascular diseases and malignancy.[1] The mortality rate from pneumonia in Sweden in 1988 was 50 per 100 000 inhabitants.[1] Estimates of the incidence of pneumonia in different populations have ranged from 3·6–12·9 persons per 1000 per year,[2–4] and approximately one fifth of patients with pneumonia are admitted to hospital.[2–4] Adult patients requiring treatment in hospital for community acquired pneumonia are mostly of middle age or older,[5 6] and fatal cases occur predominantly in this age group.[5 7]

Several factors influence the prognosis during the acute episode of community acquired pneumonia.[5 6 8–10] In a previous study[5] we found that low serum albumin levels on admission and the occurrence of a nosocomial infection were factors significantly correlated with higher mortality according to a multivariate analysis. Airway colonisation with potential pathogens and the absence of chills were also associated with death, but not to a significant degree. We have also found a high recurrence rate in patients treated in hospital for pneumonia.[11] The aim of the present study was to investigate the factors of importance for the long term prognosis after hospital treatment for pneumonia.

Methods

PATIENTS

The original patient material consisted of all patients ⩾ 18 years of age with community acquired pneumonia (n = 277) admitted to the department of infectious diseases at Danderyd Hospital, Stockholm, Sweden during a 10 month period in 1987. These patients are described in detail elsewhere.[5] Briefly, the patients had pneumonia defined as an acute lower respiratory tract disease with onset before admission to hospital and with new pulmonary infiltrates on the chest radiograph. Patients infected with HIV were excluded. For the present study we included those of the 277 patients who, on discharge from the infectious diseases department, had been classified as having pneumonia according to the International Classification of Diseases, 9th revision [ICD-9] 480-486, 487 A (n = 264). Six patients living outside Stockholm County at the time of admission to hospital were excluded because data about pneumonia relapses were unavailable, leaving a total of 258 patients for analysis. Seventeen of the patients remained in hospital and died six days to 32 months after admission. The remaining 241 patients, all of whom were dis-

Table 1 Potential risk factors and outcome variables in 241 patients discharged after hospital treatment for community acquired pneumonia

Variable	All patients studied	Recurrence of pneumonia	Death from any cause	Death from pneumonia
Mean age (years)	60·3	73·5	76·3	78·2
Serum albumin < 30 g/l	51/222 (23)	12/46 (26)	14/49 (29)	7/11 (64)
Sex (male)	103/241 (43)	21/50 (42)	22/51 (43)	7/13 (54)
Alcoholism	16/228 (7)	3/48 (6)	4/49 (8)	1/12 (8)
Smoking	88/221 (40)	16/48 (33)	19/47 (40)	3/12 (25)
Chronic obstructive pulmonary disease	31/221 (14)	8/48 (17)	6/47 (13)	0/12 (0)
Other chronic pulmonary diseases	13/221 (6)	5/48 (10)	6/47 (13)	0/12 (0)
Congestive heart failure	40/241 (17)	18/50 (36)	20/51 (39)	4/13 (31)
Diabetes mellitus	14/241 (6)	5/50 (10)	3/51 (6)	0/13 (0)
Cirrhosis of the liver	3/241 (1)	1/50 (2)	1/51 (2)	0/13 (0)
Splenectomy	3/241 (1)	1/50 (2)	0/51 (0)	0/13 (0)
Lung cancer	2/241 (1)	1/50 (2)	2/51 (4)	1/13 (8)
Non-lung malignancies	12/241 (5)	1/50 (2)	8/51 (16)	1/13 (8)
Corticosteroid treatment	18/240 (8)	7/50 (14)	8/51 (15)	1/13 (8)
Cytostatic treatment	4/240 (2)	1/50 (2)	3/51 (6)	1/13 (8)
Airway colonisation with Gram negative enteric bacteria	43/213 (20)	11/40 (28)	15/42 (36)	5/8 (62)
Airway colonisation with Candida	35/213 (16)	10/40 (25)	11/42 (26)	3/8 (38)
Other airway colonisation	9/213 (4)	0/40 (0)	1/42 (2)	0/8 (0)

Values in parentheses are percentages.

charged home, were investigated for factors of importance for long term prognosis after the hospital period. Patients who moved from Stockholm County during the study period were followed up until the date of their move.

Data on potential risk factors were prospectively collected for each patient on specially designed forms during the patient's time in hospital in 1987 (table 1)[5] and colonisation of the respiratory tract with pathogens capable of causing a secondary pneumonia was followed with repeated cultures from the oropharynx and sputum as described elsewhere.[12] From the time of the discharge of the patients until 31 October 1990 data on new episodes of pneumonia (ICD-9 480-486, 487 A) requiring admission, on total mortality, and on causes of death in hospital for the period were obtained from the central computerised data register of Stockholm County Council. This register maintains data and diagnoses for all inpatients treated in any hospital in Stockholm. Essentially the same diagnostic criteria as those used for the initial episode of pneumonia (see above) are being used in all Stockholm hospitals. Data on causes of death outside hospital were obtained from the parish authorities. In calculating the risk of dying from pneumonia after discharge from hospital, pneumonia registered both as a primary and secondary cause of death was included. One of the study patients who was readmitted with pneumonia within 14 days of discharge was assessed, not as a recurrence, but as having been treated continuously in hospital.

STATISTICAL ANALYSIS

The outcome for the 241 patients who were discharged was assessed for three end points: recurrence of pneumonia, death from any cause, and death from pneumonia. Based on earlier studies[5 9 13–15] and clinical experience, 18 independent variables from the recorded data were examined for association with the three outcome variables. For 177 of the 241 patients data were available on all 18 potential risk factors (table 1). To describe the influence of the potential risk factors, the incidences of the three end points were analysed using a proportional hazard model[16]—that is, the intensities related to the risk factors (covariates) for the end points under study were assumed to be proportional. In the analysis of the recurrence of pneumonia and death from pneumonia, individuals with recurrences after the end of the follow up period were considered as censored observations. The baseline distribution corresponding to values of zero for all covariates was modelled. For recurrence of pneumonia the Weibull distribution was fitted, while for the other two end points an exponential distribution was fitted.

The end points were studied with respect to each potential risk factor alone, as well as to each risk factor after correction for age, using age as a continuous variable. The influence of each risk factor is given as the hazard ratio with a 95% confidence interval. The model fittings were performed with the SAS LIFEREG procedure (Statistical Analysis System, SAS Institute, Cary, North Carolina).

Results

MORTALITY

The mean age of the 241 patients was 60 years (range 18–102) and 43% were male. During the mean follow up period of 31 months 51 patients died. This should be compared with the expected mortality rate of 25·9 persons in an average Swedish population of the same size and age distribution during the same time period,[17] giving a relative death risk in the patient group of 2·0 (95% confidence intervals 1·43, 3·20). Only two of the deaths occurred in patients under 50 years of age. The primary causes of death in all 51 patients are shown in table 2. In 13 patients (25% of the fatal cases) pneumonia

Table 2 Primary causes of death in 51 patients discharged from hospital after treatment for pneumonia

Cause of death	*No. of patients*
Vascular diseases	24
Lung cancer	2
Non-lung malignancies	10
Pneumonia	6
Lower respiratory infection other than pneumonia	2
Infections other than respiratory	1
Chronic obstructive pulmonary disease	1
Abdominal diseases	2
Nephrolithiasis	1
Senile dementia	1
Poisoning	1

was registered either as the primary (n = 6) or secondary (n = 7) cause of death.

RECURRENCE OF PNEUMONIA

Fifty patients had at least one relapse of pneumonia requiring hospital treatment during follow up, resulting in an incidence of pneumonia of 8·1 per 100 person-years. Eight of the patients had more than one pneumonia recurrence (one had three and two had four), so that a total of 63 episodes of pneumonia were recorded during the follow up period.

INDIVIDUAL RISK FACTORS

In the univariate analysis cardiac failure and corticosteroid treatment, together with age, correlated significantly with recurrence of pneumonia. After adjustment for age, corticosteroid treatment remained significant while congestive heart failure fell below the level of statistical significance (table 3). An analysis including both corticosteroid treatment and congestive heart failure in addition to age did not lead to any notable changes in the estimated hazard ratios. No interactions between age, corticosteroid treatment, and congestive heart failure close to significance were found. Treatment with corticosteroids also correlated significantly with death and, apart from the expected non-lung malignancies, was the only studied risk factor that remained significant in the age adjusted analysis. Seven of the 50 patients with recurrence of pneumonia and eight of the 51 patients who died were on treatment with systemic corticosteroids when they were admitted to hospital. The major reasons for steroid treatment were chronic obstructive pulmonary disease (three recurrences, five deaths) and connective tissue or joint diseases (four recurrences, three deaths).

Corticosteroid treatment did not, however, correlate with death from pneumonia. In the age adjusted analysis in this patient group airway colonisation with Gram negative enteric bacteria during the primary hospital treatment and a low serum albumin level on primary admission were statistically significant risk factors. In 43 of the patients with recurrence of pneumonia data on both colonisation and serum albumin levels were recorded. All 10 of these patients who died of pneumonia had a serum albumin level < 30 g/l, or airway colonisation with Gram negative enteric bacteria, or both (table 4).

Table 3 Risk factors for recurrence of pneumonia, death, and death from pneumonia according to the age adjusted univariate analysis*

Variable	*p*	*Hazard ratio with 95% confidence interval*
Recurrence of pneumonia		
Congestive heart failure	0·07	2·46 (0·93, 6·46)
Corticosteroid treatment	0·03	3·73 (1·10, 12·63)
Death		
Smoking	0·17	1·52 (0·84, 2·76)
Chronic pulmonary disease apart from obstructive	0·07	2·18 (0·93, 5·14)
Congestive heart failure	0·10	1·68 (0·90, 3·12)
Non-lung malignancies	0·001	3·71 (1·74, 7·88)
Corticosteroid treatment	0·01	2·68 (1·26, 5·70)
Death from pneumonia		
Airway colonisation with Gram negative enteric bacteria	0·041	4·81 (1·07, 21·85)
Serum albumin < 30 g/l	0·020	4·43 (1·27, 15·44)

*The table includes only those factors that were present in 10 or more patients with a p value of < 0·2.

Table 4 Recurrence of pneumonia and death from pneumonia correlated with serum albumin level and colonisation of the respiratory tract with Gram negative enteric bacteria

Group	*Recurrence of pneumonia*	*Death from pneumonia*	*Incidence of death/ person-years**	*95% confidence interval (incidence)*	*Mean age (years)*
Serum albumin < 30 g/l, or colonisation with Gram negative enteric bacteria, or both	19	10	0·28	(0·13, 0·51)	76·1
Serum albumin ⩾30 g/l, without colonisation with Gram negative enteric bacteria	24	0	0	(0, 0·05)	70·2

*p < 0·001 for incidence of death from pneumonia in patients with serum albumin level <30 g/l and/or colonisation with Gram negative enteric bacteria *v* those with serum albumin level ⩾ 30 g/l and no colonisation.

Discussion

This study of 241 patients discharged from hospital after treatment for community acquired pneumonia is, to our knowledge, the first attempt to assess the factors influencing the long term outcome in this category of patients. Those who are admitted to hospital with pneumonia are at risk of subsequent pneumonia and death[11] after discharge, and the results from this study show that this risk seems to be even higher in patients who are treated with corticosteroids systemically, who have low serum albumin levels on admission, or who become colonised in the respiratory tract with Gram negative enteric bacteria during their hospital stay. We have previously reported a low mortality rate for the acute episode of hospital treated community acquired pneumonia.[5] In the present study, however, we found an appreciable mortality rate during the 2·5 year follow up period, with a mortality rate twice as high as expected. In a quarter of the deaths pneumonia was registered as the cause of death, and the proportion of individuals in the patient

group where pneumonia was the primary cause of death was more than twice that in the average Swedish population > 19 years of age (11·8% *v* 4·85%).[18]

We chose our 18 independent variables based on earlier studies and our own clinical experience, but other factors of importance may have been excluded. For almost all the potential risk factors studied there was a tendency towards an increased risk of acquiring pneumonia and dying from pneumonia or other causes during the 2·5 years following discharge after treatment in hospital for pneumonia. Since many of the potential risk factors were present in only a few patients, there is a risk of "false negative" results (type II errors). This would be the case particularly for the small group of patients who died from pneumonia.

Of the individual risk factors corticosteroid treatment was significantly associated with recurrence of pneumonia and with death overall, both in the univariate analysis and after correction for age. All patients with the risk factor "corticosteroid treatment" had received steroids systemically for a long time. The association of corticosteroid treatment with the development of infection is well documented and is related to duration of therapy.[19] The immunosuppressive effects of steroids also play a part in the pathogenesis of severe opportunistic lung infections.[19–21] In acute bronchial asthma the effectiveness of corticosteroids is well established. However, the use of these agents in chronic obstructive pulmonary disease (COPD) remains controversial.[20 22] Since COPD was one of two main indications for steroid therapy in our patients with recurrence of pneumonia or death, it may be prudent to carefully consider the indication before starting systemic, regular treatment with corticosteroids in a patient with COPD.

It has been shown that the serum albumin level on admission is an important predictor of death in inpatients treated for different diseases.[23] Serum albumin levels have also been used as one of four components of a prognostic inflammatory and nutritional index showing correlation with the clinical outcome in critically ill patients[24] including paediatric clinical practice.[25] In our earlier multivariate analysis of prognostic factors influencing the short term outcome of community acquired pneumonia, low serum albumin levels on admission were significantly associated with death.[5] Colonisation of the respiratory tract with potential pathogens also seemed to be associated with death. In addition, patients with low serum albumin levels or those who became colonised had a considerably longer hospital stay and a delayed recovery. These two factors were also significantly associated with the risk of dying from recurrent pneumonia during the follow up period. Thus, in patients with community acquired pneumonia requiring admission to hospital, the presence of low serum albumin levels on admission or colonisation of the respiratory tract with Gram negative enteric bacteria are important negative prognostic factors for outcome, both for the acute episode and for recurrences after discharge. The therapeutic implications of these findings are not clear. Treatment with parenteral serum albumin[26] as well as with a dietary oral supplement[27] has been shown to reduce morbidity and improve clinical outcome in patients treated in hospital. Whether the course of the acute disease and the long term prognosis of community acquired pneumonia in patients with low serum albumin levels can be altered by protein administration remains to be demonstrated. We have now begun a prospective study in patients with community acquired pneumonia requiring admission to assess the relative importance of the different factors that influence the serum albumin level.

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Adventitia

The physician as advocate

> "It is painful for me as a physician to admit that a lawyer has saved more lives than I ever will." Mark Taylor, Physicians for a Smoke-Free Canada

For pulmonary physicians the current prime candidate for physician advocacy is tobacco. Tobacco kills more Americans every year than alcohol, cocaine, crack, morphine, heroin, automobile accidents, fires, homicide, suicide, and AIDS combined.

Reducing cigarette smoking is one of the most economical ways to prevent death. Even if tobacco consumption is reduced by an education programme which costs money to implement, reducing cigarette smoking in children is a less expensive way to save lives than spending more money on health care or reducing poverty.

The primary care physician interested in the prevention of tobacco induced lung disease can help accomplish this in several ways.

Belong to organised medical groups. Tobacco companies have almost unlimited financial resources. Physicians can only hope to have an impact by working in an organised, cohesive way, and by combining resources. Physicians still have more credibility than any other group in the health care arena.

Role model. Do not smoke or allow smoking in your surgery, and do not, for example, display magazines in the surgery which have cigarette advertisements all over the back page.

Be available as a media spokesperson. The highly paid, highly trained public relations professionals at the Tobacco Institute are continuously available to the media to take advantage of opportunities to get their point across. The physician is still highly respected and needs to be available to reiterate, not only in organised press releases but also in response to queries by the media, that cigarette smoking kills.

Be active in community education. Ninety per cent of tobacco addicts begin smoking before they graduate from high school.

Belong to or support a prohealth organisation. The American Lung Association of the American Thoracic Society has had an active advocacy role in the prevention of lung disease since the turn of the century and is now a leader in tobacco control activities.

Work for specific legislation. The 1992 Surgeon General's report concluded that "legislation that affects the supply of a demand for tobacco is an effective mechanism for promoting public health goals for the control of tobacco use." A critical national and local focus for legislative activity is to increase excise taxes on tobacco products. This serves the dual purpose of raising revenue for state coffers and reducing smoking. In 1989 the US General Accounting Report estimated that a 21 cent tax increase would result in a reduction of more than 0·5 million teenage smokers. Since people who do not start smoking as adolescents rarely become addicts, the impact of this is especially significant.

Don't be bought out. Dr John Holbrook, a Salt Lake City Professor of Medicine, was approached by a "major tobacco conglomerate" who offered to help him out with his chapter on tobacco for Harrison's *Textbook of medicine*. The tobacco industry offered him "a substantial amount of money." He reported that "it was a clear ploy to silence me. He who pays the piper calls the tune. It does influence the way we think."

The American public is waking up to the fact that tobacco causes more preventable death and illness than any other substance. They are concerned about exposure to a toxic carcinogen in the air they breathe. In Canada, attorneys were as important as physicians in the remarkable events leading to the decline in tobacco consumption. As a Canadian Cancer Society lobbyist put it: "Why spend millions on microbiologists and not on lawyers if the lawyers will be more effective in fighting the tobacco epidemic?" Physicians would be wise to recognise their responsibility to serve as advocates.

BARBARA PHILLIPS

[A fuller version of this article will appear in the *Journal of Respiratory Diseases.*]

This column is now open to allcomers for suitable contributions (maximum 600 words). We would like to keep this column running.—SGS