Severity Assessment of Lower Respiratory Tract Infection in Elderly Patients in Primary Care

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Background: Simple markers for evaluating the severity of lower respiratory tract infections (LRTI) in primary care are lacking. It is of value to examine whether the information available to the primary care physician during a patient’s initial visit can be used to assess the severity of LRTI.

Methods: The associations between different baseline variables and outcomes (survival within or more than 30 days) were investigated prospectively in a series of 950 home-living patients 65 years or older with severe LRTI that their primary care physicians suspected to be pneumonia.

Results: Twenty-one men and 17 women died (4.1%) within 30 days. According to univariate analysis, the following parameters differed \( P < 0.01 \) between the fatalities and survivors: acute aggravation of a coexisting illness, age, respiratory rate, white blood cell count, and C-reactive protein (CRP) level. According to Cox forward stepwise regression analysis (\( P = 0.01 \) for entry and \( 0.05 \) for removal), acute aggravation of a concurrent illness, respiratory rate \( \geq 25/\min \), and CRP concentration \( \geq 100 \text{ mg/L} \) were independently associated with death. The mortality rate was 2.2% if the patients had none or only 1 of the independent risk factors and 20% if they had all 3 risk factors.

Conclusions: Preceding aggravation of a concurrent illness and respiratory rate of 25/min or higher, together with an elevated serum CRP level \( \geq 100 \text{ mg/L} \), can be used as simple markers for identifying patients with the highest risk for LRTI and improve management decisions among elderly people in primary care.

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PATIENTS AND METHODS

PATIENTS

The study was carried out in association with a pneumococcal and influenza trial among persons 65 years or older in northern Finland.19 During September and October 1992, before the baseline of the study, one of the researchers (P.O.H.) visited all the municipal health centers and municipal district hospitals in the follow-up area to inform the physicians about the research design and the way of reporting patients with LRTI. The follow-up visits to the participating centers were made in the autumns of 1993 and 1994. The study population consisted of all persons 65 years or older living in 35 municipalities in northern Finland. The census on December 31, 1992, included 59,790 people, 38.8% of whom were male. The study protocol was approved by the ethical review committee of the medical faculty of the University of Oulu, Oulu, Finland. Enrollment in the follow-up study was voluntary. The physician made the diagnosis of LRTI on the basis of the patient's history and physical examination findings. During the whole study period, the primary care physicians made their decisions concerning the prescription of antibiotics and the possible referral of their patients independently.

METHODS

During the 2-year study period, 1743 cases of LRTI with signs suggestive of pneumonia were reported among the study population of 59,790 persons 65 years or older. The number of patients visiting health centers with signs suggestive of pneumonia is not known, nor is the proportion of patients with LRTI but without signs suggestive of pneumonia. Of the cases, 22 were excluded: 21 because of missing information on the day of the initial visit and 1 because of age (<60 years). One episode of suspected LRTI per patient was reported in 1424 cases. Only the first episode was included in the study for 133 patients with more than 1 episode of LRTI. Only home-living patients were included in the further analysis (1072 cases). Patients reported to be in a terminal state (10 cases) or with dementia (89 cases) were excluded because our questionnaire did not include information about whether their treatment was active or not. Of the remaining patients, those reported to be bedridden (14 cases) were excluded because our primary goal was to investigate an elderly population capable of normal daily activities. Nine patients receiving immunosuppressive treatment (>5 mg/d of cytostatics or prednisolone) were excluded.

The following patient information was recorded on the case report form by the attending physician to describe the patient's condition during the first visit: presence or absence of respiratory and other symptoms (cough, dyspnea at rest, pleuritic chest pain, acute confusion, acute deterioration of general condition, and/or acute aggravation of a coexisting chronic disease [eg, the impairment of glucose balance in diabetes or the deterioration of congestive heart failure]); duration of symptoms; date of examination; residential information (home, nursing home, municipal health center, or hospital ward); initial place of treatment (home, nursing home, municipal health center ward, or hospital ward); results of the initial physical examination (body temperature, respiratory rate, systolic and diastolic blood pressure, heart rate, and abnormal finding on chest auscultation, ie, rales); and whether the patient was in a terminal state. The patient data were complemented during the follow-up visit (or after death, if the patient died before the scheduled follow-up visit) with the basic laboratory data recorded at the initial visit: hemoglobin and C-reactive protein (CRP) levels; platelet and white blood cell (WBC) counts; erythrocyte sedimentation rate; concurrent illnesses or disabilities (eg, congestive heart failure, asthma, chronic obstructive pulmonary disease, dementia, chronic pyelonephritis, and/or type of diabetes); residence on a long-term ward; bedridden state; immunosuppressive treatment (ie, >5 mg/d of cytostatic medication or prednisolone); previous and current smoking habits; consumption of alcohol; information about possible travel abroad within the past month; final diagnosis; and, in fatal cases, whether the death was due to LRTI. To obtain valid and accurate information on the date of death and to confirm the registered coexisting illnesses, data concerning the study population were also drawn from the national register of the Finnish Social Insurance Institution, Kela. Information on dementia, dietary diabetes, alcohol abuse, and bedridden and terminal state was not available in the national register and was therefore obtained by a questionnaire. All data were stored in a computer database.

STATISTICAL ANALYSIS

The end point of the severity of LRTI was defined as mortality due to LRTI within 30 days after the first visit to a primary care physician.16 The statistical analysis was performed using the SPSS software (SPSS Inc, Chicago, Ill). Survival after the initial visit was calculated with the Kaplan-Meier method. For the analysis of categorical variables, the x2 test (or the Fisher 2-tailed exact test when appropriate) was used. The continuous variables were skewed, and median values and interquartile ranges (25th to 75th percentile) were therefore used. The association between the continuous variables and survival was analyzed using the Mann-Whitney test. For further analysis, the statistically significant continuous variables were dichotomized by selecting clinically relevant cutoff points. To identify the independent risk factors among the variables that showed statistically significant associations (P<.01) with mortality in univariate analyses, the relative risk of death was estimated using hazard ratios calculated by Cox forward stepwise regression analysis. The P value for entry into the model was .01 and for removal, .05. The patients having none or only 1 missing value of predictor variables were included for Cox regression analysis, and missing data were replaced by the geometric means of the study population: 51 mg/L for CRP level, 22/min for respiratory rate, and 9.3 × 109/L for WBC count. Similar for both sexes (Table 2). In this population with LRTI, dyspnea at rest tended to be more often observed in the patients who died within 30 days (63%) than in those who survived (48%) (P = .07; Table 2), while the

(4.1%) of whom died within 30 days after the initial visit. Of these deaths, 37% occurred within the first 7 days (Figure). Their deaths were not dependent on the initial place of treatment (Table 1). The mortality rates were
presence of rales did not statistically differ between the groups (81% vs 85%). Most of our patients with LRTI actually had real pneumonia; 83% of them had rales on chest auscultation, and 48% had dyspnea at rest during the first visit to a primary care physician. Moreover, results of a retrospective analysis of the chest roentgenograms (CXRs) showed definite pneumonia in 61% and probable pneumonia in 13%. However, we excluded the CXR findings from this study to mimic the real conditions because CXR was only available in 44% of the cases at the time of the first visit to a primary care physician in our series.

SIGNIFICANT VARIABLES ASSOCIATED WITH MORTALITY

Of the categorical variables, only acute aggravation of a coexisting illness had a statistically significant association with survival (Table 2). However, the comorbidity was not associated with mortality in univariate analysis (data not shown). Of the continuous variables, the patient’s age, respiratory rate, WBC count, and CRP values were statistically associated with death within 30 days (Table 3). When the importance of these variables was evaluated in the Cox forward stepwise regression model that included 719 cases, acute aggravation of a coexisting illness, respiratory rate (≥25/min), and CRP level (≥100 mg/L) were identified (in this order of magnitude of hazard ratios) as independent relative risk factors of death within 30 days (Table 4). The mortality rate of these patients with LRTI was 2.2% within 30 days if they had none or only 1 independent risk factor. The corresponding mortality rate was 20% if they had all 3 risk factors.

COMMENT

In this study, 2 parameters immediately available in the consulting office (preceding aggravation of a coexisting illness and respiratory rate of ≥25/min) together with an elevated serum CRP level (≥100 mg/L) at the initial visit to a primary care unit, were independently associated with the risk of death within 30 days among elderly patients with LRTI and can be used to assess the severity of LRTI.

As our results show, in most of the patients with LRTI in whom the attending physicians had primarily suspected to have pneumonia, the diagnosis of CAP was later verified by CXR. Thus, a comparison of our results with earlier reports concerning mainly CAP seemed justifiable.

It is well known that elderly patients may lack the typical symptoms of pneumonia; the earliest clues may be unspecific symptoms, such as lethargy, mental confusion, and “failure to thrive,” as well as the deterioration of a preexisting disease (eg, congestive heart failure).20

In our series, acute aggravation of a coexisting illness, such as the impairment of glucose balance in diabetes or the deterioration of congestive heart failure, was independently associated with mortality within 30 days. This
higher.9-12,14-16,18 In our study, tachypnea (with respira-
tory rates of 20/min or higher 22 to 30/min or higher 22) remained a
significant factor in univariate analysis but did not re-
main significantly associated with mortality in multivar-
iate analysis. Whether the use of CRP as a marker is recommendable in the severity assess-
ment of respiratory tract infections.

In our series, the overall rate of mortality of elderly home-living patients with LRTI within 30 days was 4%, which was lower than the percentage published in, for example, a recent meta-analysis in which the mortality rate of elderly hospitalized patients with CAP varied from 5.7% to 32.9%.23 In our primary care population, the mortality rate was even lower (2%) if the patients had no or only 1 of the independent risk factors associated with mortality. However, the mortality rate was 20% among our patients with 3 positive risk factors. The latter figure agrees with an earlier report on mortality (21%) from pneumococcal bacteremia in Finland.25

In earlier studies, controversial observations on the influence of age on the mortality in CAP have been re-
ported, with some studies supporting its importance11,17,20,27 and others not.28-30 In our series, age was a
significant factor in univariate analysis but did not re-
main significantly associated with mortality in multivar-
iate analysis. In many series, comorbidity has been shown to be an independent risk factor of mortality.16,17,22 No such association was seen in our series. In the earlier stud-
ies in which comorbidity has been recognized as a risk factor, patients with CAP have been typically treated in the hospital. In earlier studies, leukopenia and leukocy-
tosis have also been shown to be independent prognostic
markers in CAP.9,11,18,22,27 In our series, WBC count was no longer independently associated with death in CAP, did not have similar predictive value in the present series.

Because CRP level is more sensitive, decreases faster after a favorable treatment response, and is independent of age, its use as a marker instead of erythrocyte sedimentation rate has been recommended for the diagnosis and follow-up of infections.28-30 In adults with acute LRTI, a CRP level of 50 to 75 mg/L has been considered suggestive of CAP.1,13 Our results showed that a CRP level 100 mg/L or higher was independently associated with mortality in elderly patients with LRTI in primary care. Thus, our study emphasizes the importance of CRP in assessing the severity of LRTI among elderly patients in primary care. Our results also suggest that the use of CRP as a marker is recommendable in the severity assess-
ment of respiratory tract infections.

Table 3. Clinical and Laboratory Findings of Home-Living Elderly Patients With Symptomatic Lower Respiratory Tract Infection

<table>
<thead>
<tr>
<th>Variable</th>
<th>Death Within 30 d</th>
<th>Survival &gt;30 d</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No. of Cases</td>
<td>Median</td>
</tr>
<tr>
<td>Age, y</td>
<td>38</td>
<td>80</td>
</tr>
<tr>
<td>Duration of symptoms, d</td>
<td>28</td>
<td>3</td>
</tr>
<tr>
<td>Physical findings on admission</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Body temperature, °C</td>
<td>35</td>
<td>37.5</td>
</tr>
<tr>
<td>Respiratory rate, per minute</td>
<td>31</td>
<td>26</td>
</tr>
<tr>
<td>Heart rate, per minute</td>
<td>37</td>
<td>89</td>
</tr>
<tr>
<td>Systolic blood pressure, mm Hg</td>
<td>36</td>
<td>135</td>
</tr>
<tr>
<td>Diastolic blood pressure, mm Hg</td>
<td>36</td>
<td>79</td>
</tr>
<tr>
<td>Laboratory findings on admission</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hemoglobin, g/dL</td>
<td>29</td>
<td>13.0</td>
</tr>
<tr>
<td>Platelets, ×10^9/µL</td>
<td>18</td>
<td>230</td>
</tr>
<tr>
<td>Leukocytes, ×10^9/µL</td>
<td>29</td>
<td>12.2</td>
</tr>
<tr>
<td>Erythrocyte sedimentation rate, mm/h</td>
<td>15</td>
<td>52</td>
</tr>
<tr>
<td>C-reactive protein, mg/L</td>
<td>27</td>
<td>136</td>
</tr>
</tbody>
</table>

*Interquartile range (25th to 75th percentile).
†Mann-Whitney test.

Table 4. Cox Forward Stepwise Regression Analysis of Independent Risk Factors

<table>
<thead>
<tr>
<th>Variable</th>
<th>Relative Risk of Death (95% CI*)</th>
<th>P Value to Remove</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute aggravation of coexisting illness</td>
<td>No</td>
<td>1.0</td>
</tr>
<tr>
<td></td>
<td>Yes</td>
<td>2.8 (1.4-5.6)</td>
</tr>
<tr>
<td>Respiratory rate, per minute</td>
<td>&lt;25</td>
<td>1.0</td>
</tr>
<tr>
<td></td>
<td>≥25</td>
<td>2.8 (1.4-5.5)</td>
</tr>
<tr>
<td>C-reactive protein, mg/L</td>
<td>&lt;100</td>
<td>1.0</td>
</tr>
<tr>
<td></td>
<td>≥100</td>
<td>2.5 (1.2-5.1)</td>
</tr>
</tbody>
</table>

*CI indicates confidence interval.
able even in primary care patients should be investigated in a population with a larger proportion of patients undergoing such treatments.

Recently, a prognostic model for the evaluation of the severity of CAP has been described and validated in elderly hospitalized patients with CAP. We were unable to use this prognostic system, however, as some of the laboratory measurements essential for the calculation of the risk scores of individual patients, such as arterial blood gas analysis and serum urea nitrogen, were not available in the consulting offices of our primary care physicians.

We tried to find markers for the assessment of the severity of LRTI among elderly patients in primary care. These 950 home-living LRTI patients with a clinical suspicion of pneumonia were encountered by primary care physicians in their everyday practice, and the ongoing study did not influence on their treatment decisions. At least 3 parameters independently associated with mortality within 30 days are easily available: patient history (preceeding aggravation of a coexisting illness); physical findings (respiratory rate \( \geq 25/\text{min} \)); and laboratory measurement (CRP level \( \geq 100 \text{mg/L} \)). Whether these markers are generally applicable to the evaluation of the severity and treatment decisions of LRTI among elderly patients in primary care should be ascertained and validated in a new prospective study.

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REFERENCES