C-reactive protein, severity of pneumonia and mortality in elderly, hospitalised patients with community-acquired pneumonia

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Abstract

Background: increasingly, markers of systemic inflammation like C-reactive protein (CRP) levels and white blood count (WBC) are being used for assessing the prognosis of patients with community-acquired pneumonia (CAP). However, their predictive value has not been validated in populations of elderly patients.

Objective: to evaluate the prognostic value of CRP and WBC in comparison with the CURB score and the pneumonia severity index (PSI) in elderly, hospitalised patients with CAP.

Methods: the charts of all patients, aged 65 years and older, who were consecutively admitted to the Department of Geriatrics, Marienhospital Herne, Germany, for treatment of CAP between January 2001 and September 2005, were reviewed. CRP, WBC, CURB and PSI were analysed in relation to 30-day mortality.

Results: in a total of 391 patients, median age 80 years, no association was found between CRP or WBC and mortality. In contrast, the CURB score and PSI were significantly associated with mortality and treatment in the intensive care unit (ICU).

Conclusion: in elderly, hospitalised patients with CAP, admission CRP and WBC are not predictors of the prognosis.

Keywords: community-acquired pneumonia, CURB score, C-reactive protein, mortality, elderly

Introduction

Several risk scores are available for evaluating the prognosis of patients with community-acquired pneumonia (CAP). The pneumonia severity index (PSI) described by Fine et al. [1] in 1997 is widely used in the United States [2]. In Europe, CURB65—a score covering the variables acute confusion, serum urea, respiratory rate, blood pressure and age—is used to predict prognosis [2, 3]. Both tools have been validated in various populations, and, in part, in patients aged 65 years and older [4–10]. Current guidelines for the management of patients with CAP recommend the use of these scores [11–13].

Biochemical markers of inflammation have also been discussed as potentially important prognostic variables. These include, among others, the readily available C-reactive protein (CRP) level and the white blood cell count (WBC). However, the value of these markers remains unclear. A recently published study [14] reported a considerable association between CRP and mortality, describing CRP as an independent risk factor for complications and 30-day mortality. In a receiver operator characteristic curve (ROC) analysis, CRP produced a moderate performance with regard to mortality, while it outperformed CURB65 and PSI with regard to complicated pneumonia [14]. Another recent paper [15] confirmed a significant association between prognosis and CRP and WBC. In this study, however, the power of CRP and WBC to predict mortality was significantly lower than CURB65 and procalcitonin. Moreover, CRP and WBC lost their independence as predictors of prognosis in a multivariate analysis that adjusted for pneumonia severity [15].

Muller et al. [16] described a relationship between WBC, but not CRP, and mortality. Other authors report divergent...
Nursing home residents were not excluded.

admission or were receiving palliative treatment modalities.

cal confirmation of an infiltrate within the first 24 h after hospitalised within the previous 4 weeks, lacked radiol-
isation. Patients were additionally excluded if they had been ration pneumonia, pulmonary embolism or were receiving
Cases were excluded if they had stenosis-induced or aspi-
ifest infiltrate was verified and no other cause sufficiently
of clinical deterioration were included when a newly man-
ity impairment, falls, confusion, incontinence or other signs
present. Atypical cases presenting for example with mobil-

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results on the prognostic value of CRP and WBC with regard
to mortality, while a large number of the studies were pri-
marily designed as diagnostic studies [17–25]. Only one pub-
lication reported CRP and WBC in elderly patients with CAP
[10]. However, this report focused on the validation of the CURB score and assessed CRP in only 75 patients, a sample
t size too small to permit a definitive conclusion.

The aim of the present study was to compare the prognos-
tic value of CRP and WBC with that of the established risk
scores CURB and PSI in elderly, hospitalised patients with
CAP. Like Myint et al. [10], we used the abbreviated CURB
score that omits the age criterion in comparison to CURB65,
as our sample only includes patients aged ≥ 65 years.

Patients and methods

Setting

The Marienhospital is a 530-bed tertiary medical centre in
Herne, Germany. It operates departments specializing in
geriatrics, pneumology and haematology/oncology, among
others. The Department of Geriatrics mainly treats elderly
and geriatric patients requiring acute medical care. During
the study period, the management of pneumonia including
antibiotic therapy and admission to the intensive care unit
(ICU) was guided by criteria adopted from the 2001 British

Inclusion and exclusion criteria

During the period between 1 January 2001 and 15 September
2005, the charts of all patients ≥ 65 years with an ICD-10
code ‘pneumonia’ as the admission diagnosis were reviewed.
For inclusion, the radiological verification of a newly mani-
fest infiltrate was required. Patients were enrolled as present-
ing with clinically typical pneumonia, if at least two clinical
symptoms suggestive for respiratory tract infection (i.e. dys-
pnoea, cough, new or purulent sputum, fever > 38.0° C) were
present. Atypical cases presenting for example with mobi-

Definition of variables and index calculation

Data were collected on age, sex, nursing home status and
duration of inpatient treatment. The patient’s vital status
on day 30 was ascertained by inquiry with the responsible
address registration office whenever these data could not
be gathered from additional hospital resources. The infor-

mation about previous illnesses was collected as previously
described [1]. The clinical symptoms and findings collected
were pulse, systolic and diastolic blood pressure, respiratory
rate, temperature and new onset of an acute confusional state
as previously described [1].

The following laboratory values were collected: CRP, WBC, haematocrit, blood glucose, urea and sodium level on admission as well as pO2 levels and
pH values from an arterial or capillary blood gas analysis.
The chest x-ray findings were used to document any proof
of infiltrate and any pleural effusion. Since 2001, all labo-
atory values, written x-ray findings and medical reports on
patients have been available through a central server system.

Sample size calculation and statistics

The sample size was calculated using estimates of Myint
et al. [10] for the overall mortality of patients ≥ 65 years with
CAP and of Chalmers et al. [14] regarding mortality risk as
a function of admission CRP levels (CRP < 100 mg/L and
≥ 100 mg/L, respectively). Assuming a significance level of
5% (α = 0.05), a power of 80% (1 − β = 0.80), a 30-day
mortality of 20% overall and 4% in the low-risk group (group
with low CRP levels), a sample size of 49 patients for each
group was required (Fisher’s exact test). Assuming a higher
mortality risk of 8% for the group with a low CRP, a sample
size of 148 patients per group or a total of ∼300 patients
would be needed under preconditions that were otherwise
the same.

Categorical variables were stated in absolute values and in
percent, and constant variables as median, mean and standard
deviation (SD). The statistical tests on categorical variables
were performed using the χ2 test, on constant variables with
Student’s t-test. Two-tailed tests with a significance level of
5% (α = 0.05) were used for all analyses. One-way analysis
of variance (ANOVA) was used to detect differences in both
CRP and WBC as a function of the CURB score or PSI. We
used log-transformation of WBC and CRP, respectively, to
achieve a symmetrical distribution of values. Logistic regres-
sion was used to analyse the relationship between 30-day
mortality or treatment on the ICU as dependent variables
and CRP or WBC with the CURB score and other factors as
independent variables. Adjusted odds ratios (OR) with 95%

Results

A total of 438 patients ≥ 65 years with an ICD-10 code
‘pneumonia’ on admission were reviewed. Thirty patients
were excluded, as they did not fulfil the study criteria, with ambiguous x-ray findings and palliative care being the most common reasons. Seventeen cases were excluded due to missing data. The characteristics of the 391 included patients are summarised in Table 1.

The median age of the patients was 80 years (mean ± SD: 80.0 ± 8.0 years). A 30-day mortality was 19.4% (76/391 patients). A high proportion of nursing home patients (25.3%) and a generally high morbidity were striking. In terms of pneumonia severity, the majority of patients were assigned to a medium- or high-risk group. Scored by the CURB score, only 1 patient had risk class II, whereas 229 patients (58.6%) were assigned to risk class V.

CRP showed a median of 79.9 mg/L (mean 99.4 ± 87.4 mg/L), WBC a median of 11,600/µL (mean 13,037 ± 9,354/µL). In the 76 patients who died during hospital stay, the admission median CRP was 76.1 mg/L (mean 100.8 ± 87.3 mg/L), while survivors had a median CRP of 82.1 mg/L (mean 99.0 ± 87.5 mg/L, P = 0.33). The median WBC was 11,500/µL (mean 12,717 ± 6,129/µL) for deceased patients and 11,600/µL (mean 12,717 ± 6,318/µL) for survivors (P = 0.54). The median CRP and WBC on admission were not significantly different between patients requiring or not requiring ICU treatment.

Logistic regression analysis on mortality as the dependent variable produced an OR of 1.00 (95% CI 0.97; 1.03) for CRP and 1.02 (95% CI 0.99; 1.04) for WBC; when treatment on an ICU was used as the dependent variable, the resulting OR were 1.02 (95% CI 0.99; 1.05) and 1.00 (95% CI 0.96; 1.03), respectively. No relevant changes were revealed after adjusting for CURB-scored pneumonia severity, age, sex and further variables (data not shown).

A clear relationship between CRP and WBC and CURB score could not be assessed (Table 2). When scored by CURB, the median for CRP did not show any notable increase until > 2 points. There was also no meaningful increase in CRP between different PSI risk classes. No relationship between CRP or WBC and CURB or PSI, respectively, was statistically significant (Table 2).

The risk scores CURB and PSI were significantly associated with mortality (Table 3). The OR for mortality adjusted for age and sex was 1.69 (95% CI 1.21; 2.35) for the CURB score and 1.83 (95% CI 1.06; 3.14) for the PSI. The area under the curve (AUC) values from the ROC analysis for CURB and PSI with 30-day mortality as the target variable were 0.64 (95% CI 0.57; 0.71) (P = 0.001) for CURB and 0.63 (95% CI 0.56; 0.70) (P = 0.001) for PSI.

Discussion

Our data did not reveal any association between CRP and WBC and mortality. Nor did we find any relationship between
pneumonia severity and CRP or WBC. These results appear to contradict those of recent studies.

In one recent publication, Chalmers et al. describe a clear association between CRP during hospital stays and 30-day mortality and other additional clinical endpoints; the relationship remained after adjusting for pneumonia severity [14]. Although Krüger et al. confirmed a relationship between CRP and also WBC and mortality in their univariate analysis, this relationship was not maintained after adjusting for additional factors [15]. Muller et al. described an association between WBC and prognosis, but not CRP, again by univariate analysis only [16].

The major differences between our cohort and those of the studies cited are age and risk profile of the patients. Given the inclusion criterion age ≥65 years, our cohort showed a median age of 80 years which is markedly older than the populations in the studies cited [14, 15, 22]. The pneumonia severity also showed strong divergence. Based on the CURB score, 45% of our patients would be ranked as having a high mortality risk, compared with 34% [14] and 5% [15] in the other studies. Based on the PSI, just ~4% of our patients would be categorised into the favourable risk classes II or III, which contrasts with the 40% cited by Mueller et al. [22]. Furthermore, our cohort includes the highest proportion of nursing home residents. A much greater majority of patients had cardiac and cerebrovascular co-morbidities and a relevant impairment of renal function on admission compared to the other studies [14, 15, 22]. The aforementioned factors result in a markedly higher 30-day mortality rate of ~20% over comparable studies [14, 15, 22]. The aspects discussed above show that our study describes a high-risk cohort with consistently poor prognosis, which might be suggested as an explanation for the lack of any connection between CRP, WBC and prognosis.

A comparable phenomenon has been previously identified for the prognostic value of risk scores: CURB65 and PSI are comprehensively validated tools [1, 3–10, 26] that show overall good to very good performance in predicting mortality [1, 6–9, 26]. Validation studies on elderly patients have reported limited performance of the scores, which can essentially be explained by a clustering of patients in the higher risk groups [4, 5, 10]. This had previously led to various proposals for changing or supplementing the existing scores for evaluating the prognosis of elderly patients with a high mortality risk [4, 27, 28]. The performance of both scores determined in our study indeed ranks among the lowest published thus far, but is actually very consistent with comparable studies [4, 5, 10]. According to Chalmers et al. [14] and Krüger et al. [15], a weaker association exists between CRP, WBC and 30-day mortality than between CURB65 and mortality. If the same applies to our cohort, the non-significant result for CRP and WBC comes as no surprise given the weak performance of the CURB score and PSI.

Thereby, we are not arguing against the pathophysiological conclusively relationship between pneumonia severity and the extent of the pretreatment inflammatory reaction. Rather, we question the clinical importance of CRP and WBC in high-risk elderly patients. As we could reaffirm, established risk scores such as the CURB score and PSI are available that have already shown prognostic impact even in elderly high-risk patients. In view of the divergent results, the existing literature does not make recommendations for using CRP and WBC as prognostic parameters in CAP [14, 15, 22]. Instead, Krüger et al. recommend procalcitonin, not CRP or WBC, as a promising marker [15].

One limitation of our study is its retrospective design. Nevertheless, we believe that this does not detract from the validity of our data, seeing as the decisive clinical endpoint of mortality and the most important variables of interest, CRP and WBC, were easily and reliably determined by retrieval from readily available administrative and electronic records. Furthermore, the retrospective collection of data does not inherently lead to substantial disagreement with prospectively collected data, as Aujesky et al. [29] have shown for the PSI. This should likewise apply to CURB, a score essentially made up of considerably less comparable components. Our reliance on routine data, however, did not allow us to examine more recent inflammatory markers, such as procalcitonin, that are used clinically, but not routinely [15, 16, 19, 21, 22]. That such markers should be tested in high-risk patients is already a claim that Krüger et al. [15] have made in their comprehensive validation study.

In conclusion, we were not able to establish a relationship between CRP and WBC and 30-day mortality in a high-risk group of elderly, hospitalised patients with CAP. In such patients, clinicians should continue to base their prognostic assessment on clinical criteria and established risk scores such as CURB and PSI. In the future, the prognostic evaluation of CAP might be potentially improved by investigating more novel inflammatory markers, like procalcitonin, in special risk groups.

Key points
- Recent studies support the use of CRP on hospital admission as a prognostic marker in patients with CAP.
- A new report on some 390 hospitalised patients aged 65 years and older questions this recommendation, as no relationship between CRP level on admission and 30-day mortality could be found.
- In contrast, the validity of two existing prognostic tools, the CURB score and PSI, could be confirmed.
- Clinicians should not rely on CRP, but on their clinical impression and validated risk scores to assess the prognosis of elderly people with CAP.

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Conflicts of interest

The authors have no conflicts of interest to disclose.

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