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Performance of pro-adrenomedullin for identifying adverse outcomes in community-acquired pneumonia☆

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Summary *Background:* We sought to evaluate the usefulness of biomarkers—procalcitonin (PCT), C-reactive protein (CRP) and proadrenomedullin (pro-ADM)—combined with prognostic scales (PSI, CURB-65 and SCAP score) for identifying adverse outcomes in patients with community-acquired pneumonia (CAP) attending at an Emergency Department (ED).
Methods: Prospective observational study in a teaching hospital among patients with CAP. In addition to collecting data for the prognostic scales, samples were taken at the ED for assessing PCT, CRP and pro-ADM levels. We compared the prognostic accuracy of these biomarkers with severity scores to predict pneumonia related complications, using the area under the receiver operating characteristics curves (AUC), which evaluates how well the model discriminate between patients who had a pneumonia related complication or not.
Results: A total of 491 patients with CAP were enrolled, 256 being admitted to the hospital and 235 treated as outpatients. Admitted patients had higher biomarker levels than outpatients ($p < 0.001$). The SCAP score and pro-ADM level had the best AUCs for predicting pneumonia related complications (0.83 and 0.84, respectively). Considering SCAP score plus pro-ADM level, the AUC increased significantly to 0.88. SCAP score class 0 or 1 with a pro-ADM level <0.5 ng/mL was the best indicator for selecting patients for outpatient care.

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Conclusions: A new risk score combining SCAP score with pro-ADM level is useful to classify severity risk in CAP patients and hence supporting decision-making on hospital admission.

Introduction

Community-acquired pneumonia (CAP) is a major cause of morbidity in the community and imposes a huge burden on healthcare systems.[1,2] A key step in the management of CAP is the initial assessment of the severity of disease. This severity has to be identified as soon as possible, ideally at the initial presentation of the patient. An accurate assessment helps the clinician determine the site of care. To support this decision and, hence, reduce the rate of unnecessary hospital admission, validated clinical prediction rules offer a useful tool.

Several prognostic scoring systems, including the PSI[3] and CURB-65[4] severity scores, have been developed to stratify risk of mortality in patients presenting with CAP. We developed a clinical prediction rule for severe CAP, called the severe community-acquired pneumonia (SCAP) score.[5] It has been validated for the prediction of mortality in patients at low risk of mortality.[6] Some of these instruments have been used to address the challenge of identifying patients with CAP who can be safely treated as outpatients rather than requiring hospitalization,[7] and yet there are limited and controversial data regarding whether patients at low risk of dying based on severity criteria require admission to hospital.[8] The clinical staff should be able to recognize patients in need of any type of intensified monitoring and treatment, that is to say, patients who present with or are at risk of developing complications.[9] Early identification and treatment of complications, especially in the Emergency Department (ED), may improve short-term mortality.[10] However, the above are static scores and do not provide information on the host inflammatory response. The complementary use of biomarkers has been proposed as one way to improve the accuracy of clinical severity scores.[11,12] The use of biomarkers as early indicators of the strength of the inflammatory response could aid therapeutic decision making.[13–19] Current data indicate that a combination of a clinical score with a biomarker will yield the best predictions.[20,21]

The aim of our study was to evaluate the usefulness of inflammatory biomarkers, C-reactive protein (CRP), procalcitonin (PCT), and proadrenomedullin (pro-ADM), alone and in combination with the aforementioned prognostic scores (PSI, CURB-65 and SCAP scores) to select patients eligible for outpatient care and to be able to recognize patients in need of any type of intensified monitoring or treatment.

Patients and methods

Setting and study population

We prospectively followed consecutive patients with a diagnosis of CAP who visited the hospital ED and underwent an analysis of inflammatory biomarkers on the first day, between July 1, 2008, and July 31, 2009. Galdakao-Usansolo Hospital is a 400-bed teaching hospital in the Basque Country (Spain), hospital of reference that serves a population of 300,000. It is one of the networks of public hospitals of the Basque Health Service, which provides free unrestricted care to nearly 100% of the population.

Definition of pneumonia

CAP was defined as pulmonary infiltrate on chest X-ray not known to be old plus symptoms consistent with pneumonia, including cough, dyspnoea, fever, and/or pleuritic chest pain not acquired in a hospital, a nursing home or residence. Confirmation of CAP required X-ray findings suggestive of pneumonic infiltrate in the judgment of two members of the research team (PPE, AC).

Patients were excluded if they were known to be positive for the human immunodeficiency virus; were chronically immunosuppressed (defined as immunosuppression for solid organ transplantation, postsplenectomy, receiving $\geq$10 mg/day of prednisone or the equivalent for more than 30 days), were on other immunosuppressive agents, or had neutropenia, i.e., $<1.0 \times 10^9$/L neutrophils; or had been discharged from an acute care hospital, an on-site subacute care unit, or a palliative care unit within the previous 14 days, as well as any patients for whom biomarkers were not available on the first day of diagnosis.

All eligible patients were informed of the study goals and they or their legally authorized representatives gave informed consent to participate in the study. The project was approved by the hospital's ethics review board.

Data collection

This study was not an intervention study requiring implementation of standardized criteria for admission and therapy of CAP. Instead, attending physicians decided admission and treatment based on their usual practice. Specifically, patients presenting to the ED were managed in accordance with the hospital's usual clinical practice, and the final decision for hospitalization and antibiotic choice was taken by the treating physician and his or her team.

Measurements and management evaluation

Demographic and clinical data were collected from medical records by a study investigator using a written standardized questionnaire. Patient follow-up lasted for 90 days after enrolment with the goal of evaluating possible complications arising during that period of time. Outpatients were evaluated at 3–5th day by the attending physician. In addition, there is a direct on-line computer program