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Comorbidities impact on the prognosis of severe acute community-acquired pneumonia

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ABSTRACT

Community-acquired pneumonia (CAP) is a frequent cause of admission to hospital worldwide with high mortality rates. Host comorbidities may be associated not just with a greater risk of developing the disease but also with worse outcomes. In this work, the evaluation of the impact of host comorbidities on the prognosis of severe CAP patients admitted to an Intensive Care Unit (ICU) was proposed. Severity indexes, some clinical and analytic parameters at admission in ICU as well as patient comorbidities were analyzed and statistically compared with mortality. In this study, although there was no clear link between comorbidities and mortality, factors such as smoking, obesity and previous renal disease impairment seem to have an impact on the prognosis of severe CAP.

Introduction

Community-acquired pneumonia (CAP) is a common illness with an overall rate in adults of approximately 5.16–6.11 cases per 1000 persons per year.[1] It is one of the main causes of morbidity and mortality worldwide.[2–4] In developed countries, CAP is the first infectious cause of mortality with about 28% mortality within one year.[5,6] CAP is also the infectious disease with the highest health costs, as up to a third of patients needs to be admitted to hospital.[2,7] In Portugal, the hospital admission rate by CAP represented 3.7% of the total number of admissions between 2000 and 2009 with a mortality rate of 20.4%.[8] Previous studies have shown that approximately 18% of patients admitted to hospital matched the criteria for severe CAP and mortality seems to be higher in these patients.[5,9] Pneumonia incidence and severity of disease are increased in the elderly[5,10,11] which could be explained by aging of organ systems and the presence of comorbidities.[10–12] CAP is more common in men and in black people and there is a seasonal variation, with more cases occurring during the winter months.[1]

Concerning lower respiratory infections, three entities should be differentiated. CAP is an infection of the pulmonary parenchyma caused by an agent acquired in the community and should be distinguished from nosocomial or hospital acquired pneumonia (HAP) which develops at least 48 h after hospital admission, or from health-care associated pneumonia (HCAP), which occurs in patients which have been admitted to hospital during the preceding 90 days, receiving dialytic treatment during the preceding 30 days, residing in a nursing home, using home intravenous treatment or home wound care or having close contact with a person harboring multidrug resistant (MDR) pathogens.[3,13,14] These last two entities have a higher risk for MDR agent infection.[1]

Severe infection of the pulmonary parenchyma is the most frequent risk factor for acute respiratory distress syndrome (ARDS).[5] ARDS is defined by the acute onset of respiratory failure within 1 week of a clinical insult, bilateral opacities consistent with pulmonary edema on chest radiograph or computed tomography, hypoxemia with a PaO_2/FiO_2 ratio $\leq$300 mmHg on a minimum positive end-expiratory pressure (PEEP) or continuous positive airway pressure (CPAP) of 5 cmH_2O and no objective evidence of cardiac failure or fluid overload. ARDS is categorized as mild (PaO_2/FiO_2 [200–300]), moderate (PaO_2/FiO_2 [100–200]) or severe (PaO_2/FiO_2 < 100), according to the grade of hypoxemia.[15] Age and factors associated with clinical disorders may have an impact on the incidence of ARDS.[16–18] ARDS is associated with appreciable mortality, with estimates ranging from 26 to 58%, and is one of the main reasons for hospital admission.[5,7] CAP is the most common focus of infection leading to severe sepsis.[19] Sepsis is defined as a life-threatening organ dysfunction caused by a deregulated host response to infection. Sepsis can evolve to septic shock with an even higher risk of death.[20]

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CAP is more frequently caused by virus and bacteria although fungi and parasites can also be etiologic agents in some contexts. However, in many cases of diagnosed CAP based in clinical and radiologic findings, the etiology cannot be defined.[3,12] Human rhinovirus, Influenza virus and *Streptococcus pneumoniae* are the most commonly detected pathogens.[1,3] The indirect protection of adults as a result of pediatric and adult pneumococcal vaccination may potentially contribute to a slow decrease in the incidence of pneumococcal infection, but for the time being data is missing in our country.[1,3,21] *Mycoplasma pneumoniae*, *Chlamydia pneumoniae* and *Legionella pneumophila* are also common and are often referred to as "atypical" agents.[12] Agents such as *S. pneumoniae*, *Enterobacteriaceae* and *Staphylococcus aureus* are overrepresented among severely ill patients as well as patients with associated comorbidity, prior influenza infection or antimicrobial treatment.[1,3] Among patients who require admission to an ICU, *S. pneumoniae* is the most commonly detected pathogen.[1] Also, *S. pneumoniae* is the most frequently causative microorganism in smokers, particularly in invasive pneumococcal disease and septic shock.[22] Patients who are severely ill with influenza pneumonia should be evaluated for secondary bacterial infection, which is most likely to be caused by *S. pneumoniae*, group A *Streptococcus* and *S. aureus* (including community methicillin-resistant (MRSA)). *C. psittaci* should be considered in the case of exposure to birds. In patients who present certain comorbidities or some risk for HCAP, MRSA and multidrug-resistant gram-negative bacilli should be considered. MRSA is an important cause of severe, occasionally necrotizing CAP. *Pneumocystis jirovecii* is a possible agent in patients with immunodepression such as human immunodeficiency virus (HIV) infection, autoimmune diseases, transplanted or under immunosuppressive drugs. Fungal infection is an unusual cause of CAP in the immunocompetent patient, but certain fungi (e.g. *Histoplasma capsulatum*, *Coccidioides* spp.) can cause pneumonia in patients who live in or have visited endemic areas. Due to globalization, etiology of pneumonia nowadays is a dynamic issue, as evidenced by the emergence of avian influenza viruses, severe acute respiratory syndrome (SARS) and Middle East respiratory syndrome coronavirus (MERS-CoV).[1]

Epidemiological evidence suggests that, in addition to pathogen prevalence and virulence, host related factors play a critical role in determining both susceptibility to and outcome from pulmonary infections.[23,24] Many studies have sought to identify factors during the acute illness capable of predicting the outcome. Increasing age, severity of acute illness, certain pre-existing medical conditions, organ dysfunctions requiring support and emergency admission to ICU are proposed factors related to increased risk of in-hospital mortality.[5,25]

Curb-65 and Pneumonia Severity Index (PSI) are prognostic predicting systems for patients with CAP. They also help guiding the choice of the initial site of treatment, including ICU admission. The PSI score, although it is not a score easy to apply in the emergency department, has a higher discriminatory power for short-term mortality than CURB-65, especially for low risk patients.[26] The Acute Physiologic and Chronic Health Evaluation (APACHE II), the Simplified Acute Physiology Score (SAPS II) and the Sepsis-related Organ Failure Assessment (SOFA) are used in patients admitted in the ICU. The first two scores are admission scoring systems and the last one is a repetitive scoring system. The APACHE score is probably the best-known and the most widely used score. Scoring systems essentially consist of two parts: the severity score (the higher the number, the greater the severity of the condition) and the calculation of mortality risk.[25]

The aim of this study is to understand the impact of comorbidities on the prognosis of severe CAP by accessing clinical and analytic parameters, severity index scores, evolution and mortality of patients admitted to the ICU of CHSJ Infectious Diseases Service from January 2013 to December 2015.

Methods

Patients

Complete electronic medical records of patients admitted by severe CAP to an ICU from January 1st 2013 to December 31st 2015 were included. Patients with HAP or HCAP were excluded.

Data collection

Previous presence of comorbidities such as chronic diseases, noxious habits and medical immunossupression were assessed. Any documentation on medical records of HIV infection, hepatic insufficiency/cirrhosis, diabetes mellitus (DM), active malignant neoplasia, heart disease, hypertension, obesity, dyslipidemia, chronic respiratory disease, chronic kidney disease and chronic digestive disease were considered chronic diseases. Current tobacco smoking habits and high levels of alcohol consumption (>20 g of alcohol per day for men or >10 g of alcohol per day for women) were considered noxious habits. Current chemotherapy and immunossupressive drug treatment were considered medical immunosuppression. Patients with HIV infection, hepatic insufficiency/cirrhosis, DM and active malignant neoplasia, alcoholic patients and patients under medical immunossupression were considered immunodepressed. Clinical and analytic parameters were registered such as hematocrit (Ht), white blood cell count, platelet number (Plt), C-reactive protein (CRP), albumin (Alb), total bilirubin (Bil), urea (U), creatinine (Cr), glucose and sodium, lactate, pH, fraction of oxygen in the inspired air (FiO_2), partial pressure of oxygen (PaO_2) and PaO_2/FiO_2 ratio, respiratory rate, pulse, temperature, diastolic arterial pressure (DAP), systolic arterial pressure (SAP) and presence or absence of confusion and pleural effusion on first 24 h of ICU admission. Severity indexes were calculated for each patient. Patient evolution during hospitalization was assessed by discharge results (recuperation or mortality) and by the need of support for organ dysfunctions like vasopressor support (amines administration), invasive (IMV) or non-invasive (NIV) ventilatory support, renal replacement therapy (RRT) and extracorporeal membrane oxygenation (ECMO). Clinical and analytic parameters and their limit range were selected based on established severity indexes, except for C-reactive protein, albumin and lactate.

These variables were statistically compared in order to conclude their impact on mortality.

Mortality risk

Curb-65, PSI, APACHE II, SAPS II and SOFA indexes were calculated to assess the severity of pneumonia and to predict in-hospital mortality.

Statistical analysis

Data analysis was performed using the GraphPad Prism 7.02 software. Univariate comparisons of binary variables were conducted by means of continuity adjusted Y^2-tests; for continuous variables, the Mann–Whitney nonparametric two-sample test was used as values are not normally distributed. A p-value of <0.05 was considered statistically significant. Probabilities of mortality were calculated using the Kaplan–Meier estimator for each variable and hazard ratios were calculated by the log rank method with 95% confidence intervals. Median survival was defined as the time since admission to ICU and death from any cause during the time spent in hospital. Data regarding patients who were alive at the time of the analysis were censored. The severity indexes at ICU admission were also compared using these two statistical methods. Each severity index was analyzed by score comparing 'low-risk' and 'high-risk'

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