

Pneumonia with diabetes mellitus: The impact of systemic steroids and the time to first dose of antibiotics

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Abstract

Purpose: In patients with Diabetes Mellitus (DM), Community-Acquired Pneumonia (CAP) is associated with significant morbidity and mortality. The primary objective of the study was to describe the clinical outcomes and risk factors for moderate-severe CAP in hospitalized patients with DM.

Methods: We conducted a retrospective cohort study of 156 hospitalized patients with DM and moderate-severe CAP at two tertiary medical centers. Multivariate logistic and Cox regression analysis were applied to assess factors associated with complications, length of hospital stay (LOS) and mortality.

Results: Thirty one (19.9%) patients died and 81(51.9%) experienced complications during the study period. Common complications included respiratory failure (25.6%) followed by intensive care admission (16%). In the multivariate analysis, time from triage to first dose of appropriate antibiotic therapy and development of complications were associated with increased CAP related in-hospital mortality. The mean LOS was 11 days and patients developing CAP related complications 24 hours post admission had prolonged LOS. Independent risk factors for prolonged LOS included presence of complications, duration of antibiotics, and administration of systemic steroids.

Conclusion: Delayed administration of antibiotics, administration of systemic steroids and CAP related complications were associated with negative outcomes in diabetic patients with moderate-severe CAP.

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Introduction

Community-Acquired Pneumonia (CAP) is the leading cause of infection related hospitalization and a major cause of morbidity and mortality in developing countries. CAP associated mortality in hospitalized patient's ranges from 8% to 14% and up to 37% in patients admitted to the Intensive Care Unit (ICU). Several factors including age, septic shock, confusion and multipolar pneumonia have been associated with increased mortality. Validated scores, such as CURB-65 and Pneumonia Severity Index (PSI), are commonly used to predict mortality. In addition, patients with Diabetes Mellitus (DM) are at an increased risk of developing infections and complications with CAP being the most common. Studies have shown that pre-existing diabetes was associated with a higher risk of death following CAP. Factors associated with increased mortality in these patients included multipolar infiltrates, comorbidities, age, bacteremia, septic shock, infection with Gram-negative organisms and hyperglycemia. However, previous studies did not assess the impact of time from triage to administration of first dose of appropriate antibiotics in CAP complication rates LOS or mortality. Finally, clinical characteristics and outcomes of hospitalized diabetics with moderate-severe CAP are unknown. In previous work, we found that a delay in administration of first dose antibiotics in this patient population was associated with increased in-hospital mortality. However, we did not include all degrees of severity nor evaluate other outcomes. The primary objective of this study was to describe the clinical characteristics and risk factors for moderate-severe CAP in hospitalized patients with DM including outcomes such

as development of complications, LOS and in-hospital mortality.

Materials and Methods

The current study was conducted at two tertiary teaching hospitals. The Human Investigation Committee and the Institutional Review Board of Memorial University of Newfoundland and Eastern Health granted full ethics approval for the study. Given the retrospective nature, informed consent from study patients was waived. For this current study, we drew from original data published in our previous study. The medical records, including electronic copies, of all diabetic patients admitted for CAP from January 2002 to December 2007 were examined. Patients were identified through the medical record department by discharge diagnosis codes for both CAP and DM. For the study period, we included adult patients aged 18 years or older with a diagnosis of any type of DM hospitalized for confirmed CAP, PSI classes IV and V. We excluded patients with hospital-acquired pneumonia (HAP), cystic fibrosis, immune compromised condition, less than 18 years of age and those who received antibiotic therapy as an outpatient prior to presentation to the Emergency Department (ED), or required insulin during hospital stay without a prior history of DM. CAP was defined as the presence of a new infiltrate on chest x-ray and 2 or more of the following: fever, new or increasing cough or sputum production, dyspnea, chest pain, and new focal signs on chest examination. The diagnosis of DM was based on past medical history documented on the current or previous admissions. Antibiotic therapy was

considered appropriate if consistent with the Infectious Diseases of America (IDSA) and American Thoracic Society (ATS) guidelines. Complications of CAP were defined as the development of one of the following during the current hospitalization: respiratory failure, septic shock, empyema, death, and requirement for ICU admission, cardiac ischemia, arrhythmias, and other conditions. Respiratory failure was defined as a requirement of intubation or 50% oxygen requirement and septic shock was defined as a systemic inflammatory response syndrome with hypotension not responsive to adequate fluid resuscitation in the context of proven CAP and absence of other causes. Empyema was defined utilizing chest computed tomography and thoracentesis results. Cardiac ischemia was defined as the presence of typical chest pain or equivalent requiring treatment and either new positive serum troponin or ECG changes. Arrhythmias were defined as the presence of new onset or exacerbation of a preexisting abnormal rhythm on ECG (e.g. symptomatic bradycardia, atrial fibrillation, atrial flutter, multifocal atrial tachycardia, supraventricular tachycardia, torsades de pointes, ventricular fibrillation or tachycardia, and cardiac arrest). In-hospital mortality was defined as death by any cause from onset of current admission.

Results

Based on the distribution of the data, categorical variables were analyzed using chi-square test or Fisher's exact test, whereas continuous variables were analyzed by Wilcoxon rank-sum test. We divided the study patients into two groups: patients who received their first dose of antibiotic therapy 4 hours post triage. We constructed two multivariate logistic regression analyses to determine risk factors associated with in-hospital mortality and development of complications 24 hours post admission. In addition, we also constructed a multivariate cox regression analysis to determine risk factors associated with prolonged LOS using LOS in days and time to event variable as the dependent variables. We selected the independent

variables in the three models based on the clinical and statistical significance from the unvaried analysis. We considered possible interaction, assessed the goodness-of-fit of logistic regression and examined the proportional assumption of Cox regression. Statistical analysis was performed using SAS, version 9.2 (SAS Institute, Inc., Carey, NC, USA), and *p* values 0.05 were considered significant.

A total of 209 patients with CAP and DM were identified from the original study. We included 156 patients with pneumonia PSI classes IV (97 patients) and V (59 patients) in the analysis. The demographic and clinical characteristics of the study cohorts. The majority of the patients had underlying chronic medical conditions with chronic heart diseases being the most common (84.6%) followed by chronic lung diseases (39.7%).

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