



Community-Acquired Pneumonia in Patients With Diabetes Mellitus: Predictors of Complications and Length of Hospital Stay



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ABSTRACT

Background: The primary objective of the study was to determine factors associated with complications and length of hospital stay (LOS) in hospitalized adult patients with diabetes along with community-acquired pneumonia (CAP). CAP is a common infection in patients with diabetes mellitus and is associated with a significant mortality and morbidity.

Materials and Methods: This is a retrospective cohort study of 215 adult patients with diabetes who were admitted with CAP. A multivariate logistic and Cox regression analysis were used to assess factors associated with complications and LOS of CAP, respectively.

Results: During the follow-up period from admission until discharge, 94 patients (43.7%) developed complications. Respiratory failure was the most common complication (43.6%). The average LOS of study cohort was 9.47 days. In the multivariate analysis, complications of CAP were associated with time to first dose of appropriate antibiotic therapy > 8 hours since triage at emergency department (ED) (odds ratio = 3.16; 95% CI: 1.58-6.32; $P = 0.001$) and pneumonia severity index score > 90 (odds ratio = 3.52; 95% CI: 1.45-8.53; $P = 0.005$). In the multivariate Cox regression analysis, time to first dose of appropriate antibiotic therapy > 8 hours since triage at ED (hazard ratio [HR] = 0.56, $P = 0.01$), pneumonia severity index score > 90 (HR = 0.62, $P = 0.01$), presence of complications (HR = 0.53, $P = 0.002$), duration of antibiotics (HR = 0.90, $P \leq 0.0001$) and duration of symptoms prior presentation to ED (HR = 0.96, $P = 0.04$) were independently determinants of LOS.

Conclusions: Delayed administration of appropriate antibiotic therapy at ED and moderate-to-severe pneumonia were associated with both increased risk of complications and prolonged LOS in hospitalized adult patients with diabetes along with CAP.

Key Indexing Terms: Community-acquired pneumonia; Diabetes mellitus; Complications; Length of hospital stay. [Am J Med Sci 2016;352(1):30-35.]

INTRODUCTION

Diabetes mellitus (DM) is a common disease that is associated with an increased risk of infections and their complications.¹ Patients with DM are at risk of community-acquired pneumonia (CAP) and its complication due to an impaired lung function, pulmonary microangiopathy and coexisting morbidities.² Several complications may occur as a result of CAP and can be directly related to the pathogen itself or to the inflammatory process that developed with the invasion of the pathogen.³⁻⁵ Cardiovascular events are relatively commonly encountered complications of CAP. Recent studies have demonstrated that cardiac complications were associated with increased both short-term and long-term mortality in patients with CAP.^{3,4,6-8} However, the effect of cardiac complications on mortality in patients with diabetes along with CAP is unclear.

Clinical practice guidelines recommend discharging patients with CAP as soon as they are clinically stable, they have no other active medical problems and they have a safe environment for continued care.⁹ However, the length of hospital stay (LOS) varies considerably and depends on several factors such age, severity of pneumonia, complications, comorbid conditions and social and functional factors.^{9,10} There is limited existing information on CAP in patients with DM, which focused mainly on the outcome of mortality and its risk factors. However, there are no clinical studies that investigated the risk factors of complications of CAP and LOS in patients with DM.¹¹⁻¹⁴ In a previous work, we showed that time to first dose of appropriate antibiotic therapy > 8 hours since triage at emergency department (ED) was associated with increased in-hospital mortality of CAP in hospitalized adult patients with diabetes.¹² It is unclear if this association holds true between time to first

dose of appropriate antibiotic therapy and complications and LOS.

The primary aim of the current subgroup analysis of our previous study was to determine factors associated with complications and LOS of hospitalized adult patients with diabetes with CAP.

The secondary aim of the study was to determine the effect of cardiac complications on in-hospital mortality of CAP.

MATERIALS AND METHODS

A retrospective cohort study was conducted at 2 tertiary teaching medical centers. The provincial human investigations committee and the local hospital institutional review board granted full ethics approval of the study. An informed consent from study patients was not required because of the retrospective design of the cohort study. Original data of hospitalized adult patients with diabetes along with CAP from January 2002 until December 2007 was used from our previously published study.¹² Patients were identified through the medical record department of each hospital by discharge diagnosis codes of both CAP and DM. Inclusion criteria were adults aged 18 years or older, DM of any type and hospitalization with confirmed CAP. The CAP was defined as the presence of acute illness with features of respiratory tract infections (2 or more of the following: fever, new or increasing cough or sputum production, dyspnea, chest pain and new focal signs on chest examination) and the presence of new infiltrate on chest x-ray within 24 hours of presentation and verified by a radiology report. The DM was considered to be present if documented in the initial medical history.

Exclusion criteria were pre-existing infiltrate or infiltrate with alternative diagnosis or new infiltrate that developed after 48 hours of admission, cystic fibrosis, an immunocompromised condition, age less than 18 years, outpatient antibiotic therapy before presentation to the ED or insulin requirement during hospital stay without an history of DM.

The antibiotic therapy was considered appropriate if it was consistent with clinical practice guidelines.⁹ The pneumonia severity index (PSI) was used as a measure of the severity of CAP.

Complications of CAP were defined as the development of one or more of the followings during hospitalization: respiratory failure, septic shock, empyema, death or requirement for intensive care unit admission, cardiac ischemia, arrhythmias and others (eg, *Clostridium difficile*-associated infection, diabetes ketoacidosis and hypoglycemia) from onset of admission until discharge from the hospital. Respiratory failure was defined as a requirement of intubation or $\geq 50\%$ oxygen supplement. Septic shock referred to systemic inflammatory response syndrome with hypotension not responsive to adequate fluid resuscitation in the context of proven CAP. Empyema diagnosis was based on computed

tomography of the chest and thoracentesis. Cardiac ischemia was defined as the presence of documented typical chest pain or equivalent with subsequent treatment and new positive troponin or electrocardiography changes. Arrhythmias, new onset or exacerbation of a pre-existing one, was considered to be present based on electrocardiography findings during hospitalization (eg, symptomatic bradycardia, atrial fibrillation, atrial flutter, multifocal atrial tachycardia, supraventricular tachycardia, torsades de pointes, ventricular fibrillation or tachycardia and cardiac arrest).

Descriptive statistics were used to summarize the characteristics of the cohort patients. Chi-square or Fisher's exact tests were used for categorical variables, whereas *t* test or log-rank test was used to compare continuous variables. Similar to our previous study, the study patients were divided into 2 groups—patients with time to first dose of appropriate antibiotic therapy for CAP ≤ 8 hours of triage at ED and patients with > 8 hours. A multivariate logistic regression analysis was constructed to determine risk factors of complications of CAP. In the model, the complications that developed after 24 hours of admission were the dependent variables. Another multivariate logistic regression analysis was performed to determine the effect of cardiac complications (cardiac ischemia and arrhythmias) on in-hospital mortality of CAP. A multivariate Cox regression analysis to determine factors associated with LOS was constructed. In the Cox regression model, LOS in days, a time-to-event variable, was used as the dependent variable. The independent variables in all models were selected based on their clinical significance and statistical significance ($P \leq 0.05$) from the univariate analysis. The goodness of fit of the logistic regression models was assessed and the proportional hazard assumption of Cox regression model was examined. A $P \leq 0.05$ was considered significant. Statistical analysis was performed using SAS, version 9.2 (SAS Institute Inc., Cary, NC).

RESULTS

A total of 215 patients with confirmed CAP and DM were identified and included into the study. We had 6 patients who were excluded in the multivariate analysis because of missing PSI scores. The demographic and clinical characteristics of the study cohorts are shown in [Table 1](#). Most patients had comorbid conditions where heart diseases were the most common (79%). From time of presentation until discharge, 94 patients (43.7%) developed complications. A total of 68 patients (31.6%) developed complications after 24 hours of admission. Patients with complications had more severe pneumonia reflected by the high PSI score ([Table 1](#)). In total, 51 patients (23.7%) received their first dose of appropriate antibiotic therapy for CAP after 8 hours since triage at ED and 30 patients (31.9%) with complications received their first dose of antibiotic after 8 hours

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