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Original Contribution

Prognostic determinants of community-acquired bloodstream infection in type 2 diabetic patients in ED☆

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ABSTRACT

Objectives: The objective of the study is to describe the epidemiology and outcome of community-acquired bloodstream infection (BSI) in type 2 diabetic patients in emergency department (ED).
Methods: All patients admitted to the ED of the university hospital from June 2010 to June 2011 with a history of type 2 diabetes mellitus and microbiologically documented BSI were retrospectively enrolled. Demographic characteristics, Charlson comorbidity index, antibiotic therapy, clinical severity, microbiological etiology, and diabetes-related complications were recorded in a standardized form. The major outcome measure was 30-day survival. χ^2 Or Student *t* test was used for univariate analysis, and Cox proportional hazards models were used for multivariate analysis.
Results: Among 250 enrolled emergency patients with BSI, the overall 30-day mortality rate was 15.5%. Twenty-seven patients (10.7%) developed diabetic ketoacidosis (DKA), and 22 patients (8.8%) developed hyperosmolar hyperglycemic state. On univariate analysis, DKA rather than hyperosmolar hyperglycemic state was associated with adverse outcome. Other risk factors include higher mean glycated hemoglobin level, presence of underlying malignancy, long-term use of steroids, lower respiratory tract infection, and higher Charlson scores. Multivariate analysis identified 3 independent risk factors for early mortality when severity, comorbidity, age, and sex were under control: DKA (hazard ratio, 3.89; 95% confidence interval, 1.6-8.9), inappropriate antibiotics (2.25, 1.05-4.82), and chronic use of steroid (3.89, 1.1-13.2).
Conclusion: In type 2 diabetic patients with BSI, a substantial proportion of patients developed DKA. This condition was probably underrecognized by clinicians and constituted an independent risk factor for short-term mortality. Other identified risk factors are potentially correctable and may allow preventive efforts to individuals at greatest potential benefit.

1. Introduction

Patients with diabetes may carry a higher risk of bloodstream infection (BSI) [1-3]. Despite promising advances in the care of critically ill patients with severe sepsis, case fatality for diabetic patients rushed to the emergency department (ED) is 10% to 40% [1,2]. Diabetic patients with BSI are generally thought to carry a higher case fatality rate than nondiabetic patients due to risk of metabolic derangement, decreased immunity, or microangiopathic changes of vital organs.

To date, most epidemiological studies were largely comparative in design concerning the epidemiology and outcome of BSI between diabetic and nondiabetic patients [4-10]. There are few studies that examine the outcome predictors specifically among the diabetic patients in the ED. Efforts to identify the comorbid conditions that are associated with an increased risk of mortality are important because high-risk characteristics could be used as screening criteria by clinicians to focus their attention on preventing mortality in the ED.

2. Research design and methods

2.1. Study design and setting

From June 1, 2010, to June 1, 2011, we conducted a retrospective observational study in the ED at a medical center. The medical center

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was a primary and tertiary care center and has 2100 beds with annual ED census of more than 110 000 visits.

2.2. Selection of participants and data collection

The decision of obtaining blood culture was based on the clinical manifestations of systemic inflammatory response syndrome (SIRS) or clinical indication of severe infection such as pneumonia, cellulitis, abscess formation, cholecystitis, or pyelonephritis in the absence of SIRS. Patients were included in the study if they had clinically significant true bacteremia, which was defined as positive blood cultures for at least 2 sets at separate sites or 1 set for gram-negative bacterial pathogen or 1 set for gram-positive pathogen in a patient with intravascular device and clinical compatibility. Coagulase-negative staphylococci and other common skin flora isolated in single blood culture without clinical risk and compatible disease course were viewed as contamination and excluded. Patients younger than 15 years were not included in the study. All eligible patients were reevaluated by study physicians using a structured recording form. The admission course and medical records were also followed. For all eligible patients, the following data were collected retrospectively: demographic characteristics, preexisting comorbidities, exposure to indwelling catheters, initial vital signs and laboratory tests results, admission and final discharge diagnoses, and microorganisms isolated from the blood cultures. *Patient outcomes* were defined as 30-day mortality acquired either by hospital records or telephone interviews.

2.3. Identification of patients with diabetes

We ascertained the presence of diabetes in patients with a concurrent medical history of diabetes by searching the hospital-based medical records database for earlier hospitalizations with diabetes or earlier prescriptions for insulin or an oral antidiabetic drug. Those without history of diabetes but had diabetes newly diagnosed during the admission course were also eligible for analysis. Hospital records were reviewed for these patients using a detailed standardized form for diabetes-related complications.

We classified a diabetic patient as having type 1 diabetes if they were younger than 40 years at diagnosis and were treated with insulin in monotherapy. Having type 2 diabetes was classified if they were treated by diet alone or had been treated with oral antidiabetics or if they were older than 40 years at diagnosis, regardless of treatment.

Glycated hemoglobin (HbA1c) was evaluated from the value closest to the day of ED admission [10]. *Diabetic ketoacidosis* (*DKA*) was defined as presence of hyperglycemia, ketonuria or ketonemia, and metabolic acidosis with blood bicarbonate less than 18 mEq/L. *Hyperosmolar hyperglycemic state* (HHS) was defined as presence of hyperglycemia 600 mg/dL, hyperosmolarity, and absence of significant amounts of ketone bodies in the urine. Diabetic microvascular complications included nephropathy, retinopathy, or neuropathy, as documented in the hospital record and with no other suspected etiology than diabetes. Macrovascular complications included history of transient ischemic attack, stroke, angina pectoris, myocardial infarction, coronary or peripheral artery revascularization, claudication, and ulcer or amputation on the lower extremities as a result of ischemia.

Patients with history of type 1 diabetes, incomplete data recording, or hospitalization history within 48 hours of ED admission were excluded for analysis. We used the first episodes of BSI for analysis in those with repeated BSI episodes during the study period. Finally, a total of 250 patients met the inclusion criteria.

3. Definitions

Hypothermia was defined as 35.5°C, hypotension as systolic blood pressure less than 90 mm Hg, altered conscious levels as Glasgow Coma Scale less than or equal to 12, hypoxemia as pulse oxygenation less than 90%, acute renal failure as creatinine level greater than 2 mg/dL in the absence of preexisting renal disease, or creatinine greater than double of the previous creatinine level in the presence of chronic renal disease. We used modified versions of previously defined consensus criteria for defining the sepsis syndromes. *Systemic inflammatory response syndrome* was defined as the presence of 2 or more of the following: (*a*) tachycardia (heart rate, 90); (*b*) tachypnea (respiratory rate, 20) or hypoxia (oxygen saturation <95% or need for oxygen supplementation); (*c*) hyperthermia 38°C or hypothermia 35.5°C; and (*d*) leukocytosis (white blood cell count, 15 000 cells/mm^3 or bands 10%) or leukopenia (white blood cell count, <4000 cells/mm^3). *Severe sepsis* was defined as 2 or more criteria for SIRS plus organ dysfunction (altered mental status; pulmonary, oxygen saturation <90%, acute renal failure, and abnormal liver enzyme in the absence of explainable liver disease). *Septic shock* was defined as severe sepsis plus hypotension (systolic blood pressure, <90 mm Hg). The presence and source of a focal infection were classified by final discharge diagnosis as lower respiratory tract infection, urinary tract infection, biliary tract infection, liver abscess, skin and musculoskeletal infection, other intraabdominal infection, and miscellaneous. Those without a localized bacteremic source after extensive admission workup were classified as primary bacteremia. Patients were followed up until discharge. *Long-term use of steroid* was defined as use of steroid longer than 1 month in the past 3 months. The hospital's microbiology laboratory determined antimicrobial susceptibility of isolates. Therapy was considered adequate when at least 1 effective drug was included in the empirical antibiotic treatment within the first 24 hours of the admission to the ED and the dose and pattern of administration were in accordance with current medical standards. The surveillance strategy definitions did not change over the study period.

4. Statistical analysis

For univariate analysis, the comparison between groups was done using the χ^2 test or Fisher exact test for category variables and Student *t* or Mann-Whitney *U* test for continuous variables. Significant factors ($P < .20$) identified on univariate analysis were considered as potential covariates and further introduced into Cox proportional hazard regression models using backward elimination selection process. Considering the effect of sex and age on survival, these 2 factors were forced into the final model as independent variables. On Cox regression modeling, the outcome was time to death, and the censoring event was survival at the end of the 30-day follow-up. Log-log survival plots were constructed to assess the proportionality assumption underlying the Cox models. Effects of each independent predictor on outcome are expressed as adjusted hazard ratios (HRs) with 95% confidence intervals (CIs). To determine the survival difference between patients with and without DKA or HHS, survival analysis was performed using Kaplan-Meier survival curves, and the significance was tested using the log-rank tests. All tests were 2 tailed, and $P < .05$ was considered statistically significant. All data were analyzed with SPSS software for Windows (Release 13.0; SPSS, Inc, Chicago, IL).

5. Results

5.1. Patient population

During the 1-year study, 95 630 patients were admitted to the adult ED. A total of 964 episodes had clinical significant positive results for blood culture, of which 285 had a confirmed history of diabetes. Of the 285 episodes, 14 episodes were excluded as repeated infection, 9 excluded as nosocomial infection, 5 excluded as type 1 diabetes, and 7 excluded as incomplete medical records of diabetes-associated comorbidities. Finally, a total of 250 patients entered the analysis. The distribution of age, sex, and 30-day mortality of the excluded 35 cases with incomplete data were comparable with those of the included patients.