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The prognostic significance of admission blood glucose levels in elderly patients with pneumonia (GAP Study)

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ABSTRACT

Aims: Evaluate the association between admission blood glucose (ABG) and short and long-term mortality following hospitalization for pneumonia of elderly patients with and without diabetes mellitus (DM).
Methods: Observational data derived from the electronic records of hospitalized patients ≥65 years, admitted for pneumonia between January 2011 and December 2013. ABG levels were classified to categories: ≤70 (low), 70–110 (normal), 111–140 (mildly elevated), 141–199 mg/dl (moderately elevated) and ≥200 mg/dl (markedly elevated). Main outcomes were all-cause mortality rates at various time points.
Results: Cohort included 2164 patients, 743 with DM (mean age 81, 53% male) and 1421 without it (mean age 83, 52% male). There was a significant interaction between DM, ABG and mortality ($p \leq 0.05$). In patients without DM, compared with normal ABG, in-hospital and 30-day mortality rates (adjusted hazard ratio, 95% CI) were higher with moderately (1.5 and 1.4, respectively, $p < 0.05$) and markedly elevated ABG (2.7 and 1.9, respectively, $p < 0.05$). Long-term results were similar at 12 and 36 months (1.3 and 1.8, respectively, $p < 0.05$, for moderately and markedly elevated ABG).
Conclusion: In elderly non-diabetic patients hospitalized for pneumonia, moderately and markedly elevated ABG is associated with increased short- and long-term mortality. In diabetic patients there is no association between ABG and mortality.

1. Introduction

Infectious diseases are a major cause of morbidity and mortality in patients with diabetes mellitus (DM), probably due to abnormalities of host response, mainly in neutrophil chemotaxis, adhesion and intracellular killing (Baiju & Janet, 2003; Boyko, Fihn, Scholes, Abraham, & Monsey, 2005; Hamilton et al., 2013; Muller, Gorter, Hak, et al., 2005; Thomsen et al., 2005). Elevated admission blood glucose (ABG) levels during acute illness are associated with poor outcomes in patients with and without DM following admissions for several conditions: ischemic or hemorrhagic stroke (Capes, Hunt, Malmberg, Pathak, & Gerstein, 2001), surgery (Golden, Linda, & Frederick, 1999), trauma (Yendamuri, Fulda, & Tinkoff, 2003), heart failure (Barsheshet, Garty, Grossman, et al., 2007; Kosiborod, Inzucchi, Spertus, et al., 2009), pulmonary embolism (Scherz, Labarère, Aujesky, & Méan, 2012) and acute myocardial infarction (Capes, Sarah, & Hertzel, 2000; Timmer, van der Horst, Ottervanger, et al., 2004; Yang, Song, Bin, et al., 2013).

Pneumonia-related mortality rates range between 5% and 10% in the short-term, and 20% to 65% of patients hospitalized with pneumonia die within 5 years (Johnstone, Eurich, Majumdar, Jin, & Marrie, 2008). Up to 25% of patients with pneumonia have DM (Abourizk, Vora, & Verma, 2004). Hyperglycemia-associated impairment in host defense functions may increase the risk for respiratory tract infection or lead to greater pneumonia severity, compared with euglycemia, resulting in increased mortality rates (Kornum et al., 2007, 2008; Koziel & Koziel, 1995). Blood glucose levels at admission are readily available for most hospitalized patients, and may predict the short and long-term outcomes of patients admitted for pneumonia.

Our objective was to evaluate the association between ABG levels in elderly patients with and without DM and all-cause short and long-term outcomes following hospitalization for pneumonia.

2. Methods

Historical prospective data were extracted from the electronic medical records of all elderly patients who were admitted to the medical wards in Rabin Medical Center, Israel, between January 1, 2011 and December 31, 2013. Inclusion criteria were age ≥65 years with a principal discharge diagnosis of pneumonia. Diagnosis of

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pneumonia was based on patients' complaints, physical examination, laboratory results and imaging studies. In case of a recurrent admission for pneumonia, the first admission in that time period was considered the index hospitalization. Patients with nosocomial pneumonia were also included. Patients without a documented ABG levels were excluded.

Rabin Medical Center, encompassing Beilinson and Golda-Hasharon campuses, is a tertiary-care facility with more than 1300 beds. Most of the admissions to the 10 medical wards are through the emergency department, and all patients' data are recorded in electronic medical charts, based on the same database platform used in community primary care facilities. Mortality data were obtained from the hospital's mortality database, updated from the Ministry of the Interior Population Registry. We collected mortality data until June 1, 2015.

Patients were stratified into those with pre-existing DM, if their medical record included a diagnosis of DM or use of any oral hypoglycemic agent, glucagon-like peptide agonist, or insulin at the time of admission, and to those without DM.

ABG levels, defined as the blood glucose level closest to the patient arrival time, within the first 24 h of the admission date, were classified into the following five categories: <70, 70 to 110, 111 to 140, 141–199, and ≥200 mg/dl. Blood glucose measurements were based on Point Of Care-Blood Glucose measurements using bedside glucometers or serum glucose levels derived from venous blood samples.

We have collected data regarding co-morbidities, according to diagnoses as defined in the medical records, including: hyperlipidemia, hypertension, ischemic heart disease, chronic heart failure, chronic renal failure, cerebrovascular disease, chronic obstructive pulmonary disease, asthma, interstitial lung disease, and inflammatory bowel disease. We included patients with immunosuppression.

In this Glucose Admission in Pneumonia (GAP) study the primary outcome was the rate of all-cause mortality in the short-term (in-hospital and 30 days) and long-term (12, 24, and 36 months) after admission of elderly patients for pneumonia.

3. Statistical analysis

The statistical analysis was generated using SAS Software, version 9.4 of the SAS System for PC, Copyright 2002–2012. SAS Institute Inc. and all other SAS Institute Inc. products or service names are registered trademarks or trademarks of SAS Institute Inc., Cary, NC, USA.

Continuous variables were presented as mean ± SD; categorical variables were presented as (n, %). T-Test was used to compare the value of continuous variables between study groups and Chi-Square was used to value of categorical variables between study groups. Cox proportional hazards model was used to assess the effect of study variables on survival, including age, gender, smoking, alcohol, corticosteroid treatment, ischemic heart disease, congestive heart failure, hypertension, and cerebrovascular disease, as well as for interaction between DM and glucose levels. Since this interaction was significant ($p < 0.001$), the Cox model was rerun by DM groups. This analysis proved a significant association between ABG levels and in-hospital, 30-day, 12, 24 and 36-month mortality rates in patients without DM, but in the group of patients with DM there was no significant association at any of these time points ($p > 0.05$). Subsequently, we focused our data analyses on the group of patients without DM.

As we did not have data regarding the severity of pneumonia, we used the length of admission as a surrogate marker for severity, and evaluated the association between length of admission and 30-day mortality, 1-, 2- and 3-year mortality, assuming prolonged length of stay in patient with severe infection. We focused on 30-day mortality since in-hospital mortality rates may skew the results, as mean length of admission may be shortened with in-hospital mortality.

We had complete data for all the study variables, other than BMI and smoking. No imputation for missing data was done because missing at random cannot be assumed.

Due to the small number of patients with low ABG levels, we did not analyze the data for this group.

4. Results

4.1. Study cohort

Among 73,796 admissions to the medical wards during the study period, the final cohort comprised of 2164 patients admitted with pneumonia with complete data (Fig. 1). Mean age of the cohort was 82 years (65–110 years), 1093 were men (51%) and 1421 (66%) did not have pre-existing DM. Compared with diabetic patients, those without DM were older (mean age 83 ± 8 vs. 81 ± 8, $p < 0.001$). Rates of hypertension, hyperlipidemia, ischemic heart disease, congestive heart failure, chronic renal failure and cerebrovascular disease were significantly higher in the group of patients with pre-existing DM (Table 1). The mean total follow-up after discharge was 520 days (median, 397 days).

Most patients without DM had mildly elevated ABG levels (37%) or normal ABG levels (28%), while markedly elevated ABG levels were much less common (9%). However, most of the patients with DM had markedly elevated ABG levels (41%), or moderately elevated ABG levels (32%). The total number of patients with low ABG levels was very small (12 patients in each group, 2% and 1%, with and without DM, respectively) (Fig. 1).

In-hospital mortality rates in the group of patients with normal, mildly, moderately and markedly elevated ABG levels were 17%, 16%, 21% and 28%. 30-day mortality rates were 27%, 25%, 33% and 39%. 12, 24 and 36-month mortality rates were 47%, 55% and 58% with normal ABG levels, 43%, 51% and 54% with mildly elevated ABG levels, 51%, 59% and 63% with moderately elevated ABG, and 57%, 64% and 69% with markedly elevated ABG levels.

In the group of patients with normal or mildly elevated ABG levels, in-hospital mortality rates were similar in patients with and without DM, but 30-day mortality rates and long-term mortality rates were higher in the group of patients with DM. However, with moderately or markedly elevated ABG levels, short- and long-term mortality rates were higher in the group of patients without DM, compared to patients with DM (Table 2).

4.2. Patients with DM

In the group of patients with DM there was no significant association between ABG levels and short- and long-term mortality rates without statistically significant difference in adjusted hazard ratio ($p > 0.05$).

4.3. Patients without DM

In patients without DM, there was a statistically significant association between ABG and short (in-hospital and 30 days) and long-term mortality (12, 24 and 36 months) ($p < 0.0001$ for all comparisons).

4.3.1. Baseline characteristics

In the group of patients without DM (n = 1,421), 28% had normal ABG levels (n = 392), 37% had mildly elevated ABG levels (n = 521), 26% had moderately elevated ABG (n = 372), 9% had markedly elevated ABG levels (n = 124) and only 1% (n = 12) had low ABG levels. There was no significant difference between the different ABG categories in rates of malignancy, hyperlipidemia, hypertension, and all other comorbidities. The mean age of patients without DM with markedly elevated ABG levels was 85 years, compared with a mean age of 82, 83 and 84 in the groups of patients with normal, mildly and