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Effect of short- and long-term diabetes control on in-hospital and one year mortality rates in hospitalized patients with diabetic foot

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ABSTRACT

Introduction: It remains unclear whether diabetic patients with diabetic foot complications benefit from strict glycemic control during hospitalization. The present study investigates the effect of short- and long-term diabetes control on hospital outcomes including: in-hospital and one year mortality rates, length of hospital stay and the rate of repeated admissions.

Methods: Type 2 diabetic patients (n = 341) were hospitalized for diabetic foot complications at Wolfson Medical Center over a 5 year period (2008–2012). The adequate short-term glycemic control was defined as average glucose levels between 110 and 180 mg/dL. HbA_{1c} values below 7% were defined as adequate long-term glycemic control.

Results: The average glucose levels during hospitalization were 179 ± 45 mg/dL and 40% of the measurements were between 110 and 180 mg/dL. Mean admission HbA_{1c} levels were 8.43% ± 2.26%, and 31% of the values were below 7%. The mean length of hospital stay was 24.3 ± 22.6 days, 15.0% of the patients needed surgical intervention during admission, the in-hospital mortality rate was 10.3%, and the rate of 1-year readmission was 25.1%. Adequate diabetes control during hospitalization was not significantly associated with reduced in-hospital mortality (hazard ratio, 0.454, 95% confidence interval 0.186–1.103, p = 0.081). However, adequate diabetes control during hospitalization lead to significantly decreased one year mortality (hazard ratio, 0.269, 95% confidence interval 0.707–0.101, p = 0.009). Adequate diabetes control during hospitalization did not affect the length of hospital stay or the rate of repeated admission.

Conclusions: Improved glucose control during hospital admission (levels between 110 and 180 mg/dL) was associated with reduction of one year mortality.

1. Introduction

The available epidemiologic and clinical trial data support the hypothesis that improved glycemic control reduces microvascular complications as well as incidence of cardiovascular events in patients with type 2 diabetes mellitus [1–3]. Based on these studies, European Association for the Study of Diabetes (EASD) and American Diabetes Association (ADA) recommend a strict metabolic control with HbA_{1c} < 7.0% for most adults with diabetes [4,5]. The ACCORD and ADVANCE trials demonstrated an increased mortality among patients who were randomized to receive intensive glycemic control. Hence, a less stringent HbA_{1c} goal was suggested for patients with a history of severe hypoglycemia, a limited life expectancy and advanced diabetic

complications [6]. Patients with a history of diabetic foot are considered to be a high-risk population for increased cardiovascular and all-cause mortality [7–9]. Recent clinical trials evaluating survival in type 2 diabetes patients with hard-to-heal foot ulcers, have suggested that intensive therapy may be associated with increased short- as well as long-term all-cause mortality in patients with HbA_{1c} levels below 7.5% [10]. Whereas optimized metabolic control undoubtedly plays a major role in preventing progression of microvascular as well as macrovascular complications, it is not clear whether patients with diabetic foot benefit from strict glycemic control. Thus, the clinical impact of short- and long-term diabetes control in this population deserves further investigation.

The present study was designed to investigate effect of short- and

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long-term diabetes control on hospital outcomes including in-hospital and one year mortality, length of hospital stay, and rate of repeated admission, in hospitalized patients with diabetic foot.

2. Methods

The study group consisted of 341 type 2 diabetic patients hospitalized from January 2008 through December 2012 in Wolfson Medical Center due to the diagnosis of diabetic foot complications. Most of the patients were hospitalized in the Diabetic Foot Unit.

The medical files of the patients were evaluated for comorbid conditions, concomitant medication and biochemical parameters. Wolfson Medical Center has a centralized glucometer system (Accu-Check Inform, Roche Diagnostics, Indianapolis, IN, USA) since 2007, as part of a hospital-wide treatment plan for diabetes patients. All performed glucose measurements are stored in the patients' computerized health records. The medical records were reviewed, and information regarding HbA_{1c} levels and all glucose measurements were recorded.

Short- and long-term diabetes control was defined by average glucose during hospitalization and HbA_{1c} at admission. Adequate short-term glycemic control was defined as average glucose levels during admission between 110 and 180 mg/dL. HbA_{1c} values below 7% were defined as adequate long-term glycemic control.

Adequate short and long-term glycemic control were defined prospectively based on treatment goals recommended by the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD) in 2012 for adults with type 2 diabetes. Recently, a less stringent HbA_{1c} goal was suggested for patients with advanced diabetic complications. Thus, today it is not clear whether patients with diabetic foot have similar targets and can benefit from strict glycemic control.

Patients were divided into two groups according to short-term glycemic control defined by average glucose levels during admission. Group 1 consisted of 206 diabetic subjects with poor short-term glycemic control and Group 2 contained 135 participants with adequate short-term glycemic control.

Additionally, diabetic subjects were divided into two groups according to HbA_{1c} levels: Group 1 consisted of 235 participants with poor short-term glycemic control (HbA_{1c} > 7%) and Group 2 contained 106 diabetic subjects with adequate long-term glycemic control (HbA_{1c} < 7%).

The hospital outcomes of patients with diabetic foot included: in-hospital and one year mortality, length of admission and one year readmission rate.

The study was approved by the local Institutional Review Board and was carried out in accordance with the [Declaration of Helsinki](#), as revised in 2000.

3. The Glucose monitoring system

The automated glucometer (Accu-Check Inform, Roche Diagnostics, Indianapolis, IN) was located in each inpatient department. The handheld device is powered by a rechargeable lithium battery, and its base unit can be mounted on a wall or desktop. Measuring 3.6 × 9.6 × 19.4 cm, the device has a curved target area for blood application and blood is pulled to the test strip via capillary action; however, blood does not actually enter the meter, reducing the risk of contamination. Data may be entered using a touch screen and/or bar code scanner. As many as 4000 results may be stored in the memory with up to three, user-defined or free text comments per test. Test results are stored with a test identifier code (meter serial number), patient identification, identification of the clinician performing the test, and date and time stamp. Precision of the Accu-Chek in critically ill hospitalized patients has been reported. Data are transmitted and downloaded automatically to the central database of the hospital's biochemistry laboratory. The information system (Roche Cobas IT 1000,

Roche Diagnostics) permits authorized personnel to access, monitor, and analyze data, which can be downloaded in spreadsheet format for the assessment of temporal trends and the identification of out-of-range values.

4. Statistical analysis

Analysis of data was carried out using SPSS 9.0 statistical analysis software (SPSS Inc., Chicago, IL, USA, 1999). For continuous variables, such as hemodynamic and chemistry measures, descriptive statistics were calculated and reported as mean ± standard deviation. Normalcy of distribution of continuous variables was assessed using the Kolmogorov–Smirnov test (cut off at $p = 0.01$). Categorical variables such as comorbidities and prescribed medications were described using frequency distributions and are presented as frequency (%). Cox proportional hazard regression models were applied to study the independent association between average glucose levels, HbA_{1c} level and in hospital and one year mortality. The results of these Cox proportional hazards models are presented as hazard ratio, with 95% confidence interval. We developed regression models for the dichotomous (e.g., death within one year) and linear variables (e.g., duration of hospitalization), in order to examine the association between diabetic control levels during hospitalization and length of hospitalization, death risk during hospitalization, and death within a year.

5. Results

The study group consisted of 341 patients (mean age 67.8 ± 12.7 years, 66% males) with type 2 diabetes hospitalized over 5 years (2008–2012) at Wolfson Medical Center with a diagnosis of diabetic foot. The average glucose level during admission was 179 ± 45 mg/dL and 40% of the measurements were between 110 and 180 mg/dL. The mean admission HbA_{1c} level was 8.4%, whereas 31% of the HbA_{1c} values were below 7%. The mean length of hospital stay was 24.3 ± 22.6 days, the rate of one year readmission was 25.2% and in-hospital mortality rate was 10.3%.

5.1. Between group comparisons by short term glycemic control

Demographic and clinical characteristics of the two groups are presented in [Table 1](#). As can be seen, there were no significant differences between the two groups in terms of age, sex, gender distribution, presence of cardiovascular risk factors and concomitant medications. As expected, mean HbA_{1c} as well as average glucose levels were significantly higher in Group 1 compared to Group 2. Although CRP levels did not differ significantly between the groups at admission, at the end of the hospitalization, CRP levels were significantly lower in Group 2 than in Group 1 ($p = 0.190$ and $p = 0.044$, respectively). Hypoglycemic events were significantly higher in Group 2 compared to Group 1 (48.5% vs. 22.5%, $p < 0.001$). As can be seen in [Fig. 1A](#), using the Cox regression analysis, adjusted for age, sex and HbA_{1c} levels we found that adequate diabetes control during hospitalization was significantly associated with one year mortality (hazard ratio, 0.269, 95% confidence interval 0.101–0.717, $p = 0.009$). Adequate diabetes control during hospitalization was not significantly associated with reduced in-hospital mortality (hazard ratio, 0.454, 95% confidence interval 0.186–1.103, $p = 0.081$) and did not affect the repeated admission during one year follow-up (hazard ratio, 0.791, 95% confidence interval 0.463–1.349, $p = 0.389$).

5.2. Between group comparisons by long term glycemic control

Demographic and clinical characteristics of the two groups are presented in [Table 2](#). As can be seen, there were no significant differences between the two groups in terms of age, sex, gender distribution, presence of cardiovascular risk factors, concomitant medications, CRP

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