Plasma Glucose at Hospital Admission and Previous Metabolic Control Determine Myocardial Infarct Size and Survival in Patients With and Without Type 2 Diabetes

The Langendreer Myocardial Infarction and Blood Glucose in Diabetic Patients Assessment (LAMBDA)

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Hyperglycemia at the time of hospital admission has been associated with shorter survival after acute myocardial infarction in patients both with and without diabetes (1–5). It is not fully understood whether this is due to the acute development of stress hyperglycemia or to the quality of long-term metabolic control before the event (6). Moreover, the mechanisms by which hyperglycemia in the postinfarction period affects survival are largely unknown. In the present study, the LAMBDA (Langendreer Myocardial Infarction and Blood Glucose in Diabetic Patients Assessment) database was used to investigate the influence of acute (plasma glucose determined on admission) and long-term (HbA_{1c} [A1C]) glycemic control on the size of myocardial necroses and prospective long-term survival after >3.5 years.

RESEARCH DESIGN AND METHODS

— Clinical data of all patients admitted to the Department of Medicine of Ruhr-University, Knappschafts-Krankenhaus, Bochum (Langendreer), between 1 January 1991 and 30 June 1997 who were diagnosed with acute myocardial infarction were collected as described (4,7). All patients, their nearest spouses, and the responsible general practitioners were contacted after >3.5 years to obtain information on the vital status. In the present analysis, data from 227 type 2 diabetic and 287 nondiabetic patients were examined. Both groups were divided in tertiles according to the plasma glucose concentrations determined at hospital admission. All creatine kinase (CK) activities (including CK_{MB} [muscle/brain]) were determined twice daily at 12-h intervals in each patient. All patients received standard clinical care including monitoring of vital functions on an intensive care unit during the initial hospital stay and thrombolytic treatment according to current guidelines. Life table analysis was performed according to Kaplan and Meier. Contingency table analysis (χ^2 and Fisher's exact test) and repeated-measures ANOVA were used to analyze categorical or continuous variables, respectively. In case of significant differences between groups, individual values were compared by one-way ANOVA followed by Duncan's post hoc test.

A multivariate proportional hazards Cox regression analysis, including sex, age, BMI, diabetes duration, A1C, antidiabetic treatment, hypertension, smoking status, history of myocardial infarction, duration of thoracic pain, and cardiovascular medication, was carried out separately in type 2 diabetic and nondiabetic patients as well as in the entire study population.

RESULTS

— In patients with type 2 diabetes, the proportion of female patients was higher in the highest glucose tertile compared with the lowest glucose tertile (55.6 vs. 42.1%, $P = 0.047$). As expected, patients in the highest glucose tertile showed the highest A1C concentrations ($P < 0.0001$). Plasma creatinine concentrations were higher ($P = 0.024$) and total and LDL cholesterol concentrations were lower in the subgroup with the highest glucose levels ($P < 0.05$). The duration of known diabetes was longer in the tertiles with higher glucose levels than in the low-glucose subgroup (11 ± 7 vs. 5 ± 4 years, $P < 0.0001$). Patients in the highest plasma glucose tertile were more likely to receive sulfonylureas or acarbose treatment ($P < 0.05$). In the nondiabetic patients, no differences regarding sex, BMI, and the history of previous acute myocardial infarction were found between the subgroups. However, the proportion of patients with known arterial hypertension was higher in the high-glucose subgroup (38.1%) than in the lowest glucose tertile (25.5%, $P = 0.044$). Total cholesterol levels were lower in the high-glucose tertile ($P = 0.026$), but there were no differences in A1C concentrations between the subgroups. No differences between the subgroups were seen in the previous use of drugs affecting cardiovascular function both in diabetic and nondiabetic patients.

Survival after acute myocardial infarction

The plasma glucose concentrations determined at the time of hospital admission strongly predicted long-term survival after the acute myocardial infarction in patients both with and without type 2

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Abbreviations: CK, creatine kinase.

A table elsewhere in this issue shows conventional and Système International (SI) units and conversion factors for many substances.

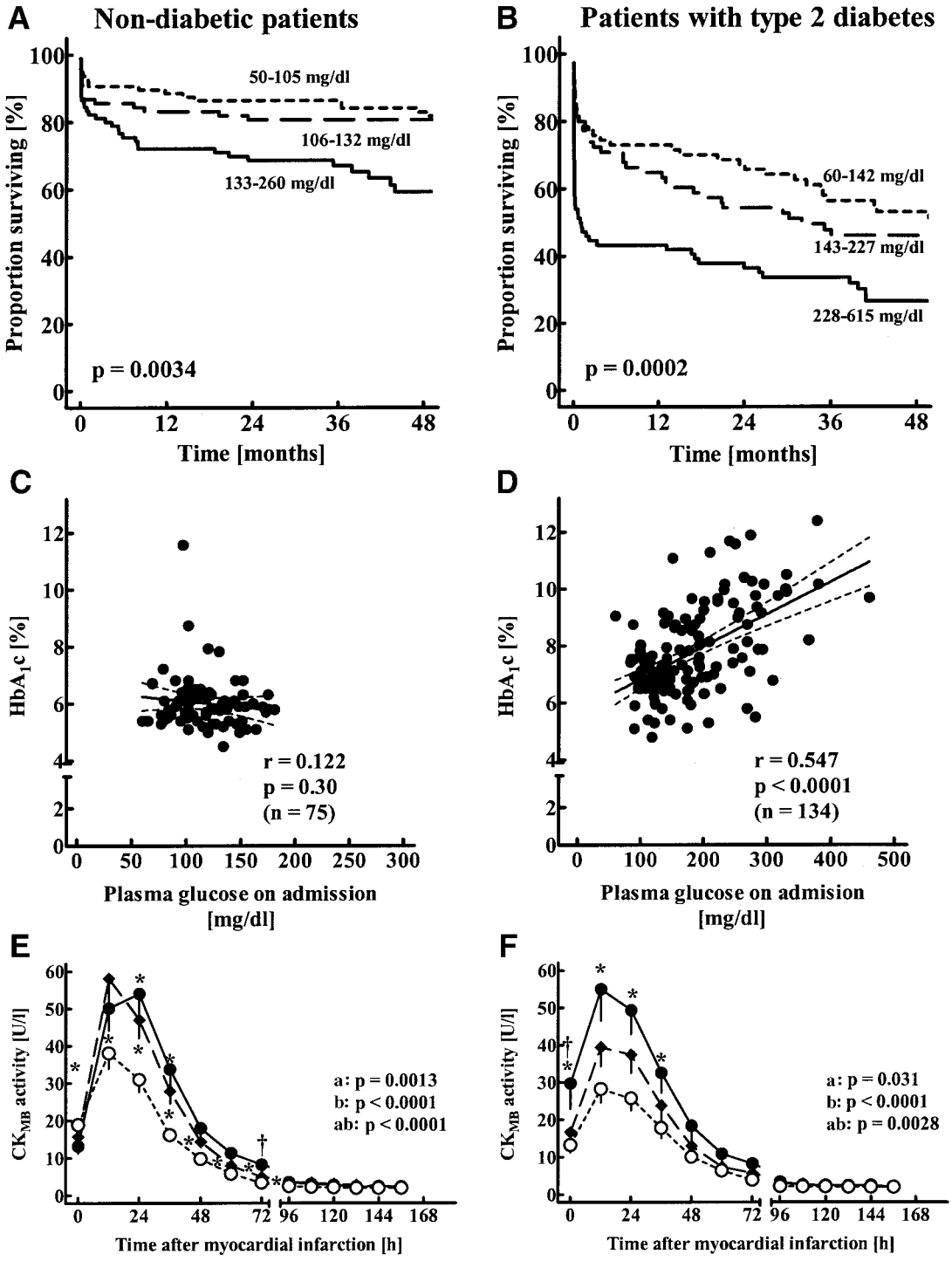

Figure 1—A *and* B*: Survival analysis (Kaplan-Meier method) of nondiabetic and type 2 diabetic patients admitted to the hospital with acute myocardial infarction. Patients were grouped according to tertiles of plasma glucose concentrations determined upon hospital admission.* C *and* D*: Correlation of individual A1C values with plasma glucose concentrations determined at hospital admission in nondiabetic and type 2 diabetic patients. Dotted lines indicate the 95% CI for the regression lines.* r *= correlation coefficient by linear regression analysis.* E *and* F*: Increments of CK_{MB} after hospital admission for acute myocardial infarction in nondiabetic and type 2 diabetic patients grouped according to tertiles of plasma glucose concentrations. Data are presented as means ± SEM.* P *values were assessed by repeated-measures ANOVA and denote differences between tertiles (a), differences over time (b), and differences due to the interaction of group and time (ab). *Significant differences (*P *< 0.05) from the lowest glucose tertile at individual time points; †significant differences from the intermediate glucose tertile (ANOVA plus Duncan's post hoc tests).*

diabetes (Fig. 1). In both groups, the intertertile differences in plasma glucose levels were most prominent on the day of hospital admission. However, while the differences in both fasting or postprandial plasma glucose levels between the subgroups remained significant until 14 days after hospital admission in the diabetic patients ($P < 0.05$), the differences could

no longer be detected after >3 days in the nondiabetic patients. A strong positive correlation between plasma glucose concentrations determined at hospital admission and A1C values was found in type 2 diabetic patients ($r = 0.55$, $P < 0.0001$) but not in nondiabetic patients ($r = 0.12$, $P = 0.30$; Fig. 1).

In both patients with and without diabetes, increments in plasma CK and CK_{MB} were higher in the subgroups with higher plasma glucose at hospital admission (Fig. 1), suggesting larger myocardial necroses with increasing levels of glycemia. In addition, significantly positive correlations of peak CK (or CK_{MB}) activities and admission glucose concentrations were found in both groups (details not shown).

Multivariate regression analysis

In a multivariate proportional Cox regression analysis, the association between plasma glucose concentrations and the survival after acute myocardial infarction remained valid in both patient groups. The increase in the relative risk (95% CI) per increment of 50-mg/dl plasma glucose concentrations was 1.42 (1.31–1.52, $P < 0.0001$) in type 2 diabetic patients and 1.54 (1.19–1.89, $P = 0.0024$) in nondiabetic patients.

CONCLUSIONS — The present data demonstrate that *1*) in patients both with and without type 2 diabetes, hyperglycemia at the time of acute myocardial infarction is associated with shorter prospective survival; *2*) patients with high glucose concentrations at hospital admission develop larger myocardial necroses (peak CK and CK_{MB} increments); and *3*) in patients with type 2 diabetes, long-term metabolic control predicts plasma glucose levels at the time of hospital admission and therefore determines prospective survival. In nondiabetic patients, however, hyperglycemia at admission seems to represent a stress response that is also associated with larger myocardial necroses and an adverse outcome. Thus, even though the survival benefit achieved by the use of insulin-glucose infusion regimens is still controversial (8–10), these findings emphasize the need for further prospective intervention trials to investigate the impact of tight glucose control on survival after myocardial infarction.

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