Oral Glucose Tolerance Test: A Reliable Tool for Early Detection of Glucose Abnormalities in Patients With Acute Myocardial Infarction in Clinical Practice

A report on repeated oral glucose tolerance tests from the GAMI Study

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OBJECTIVE — Previously undetected glucose abnormalities are common in patients with acute myocardial infarction (AMI). We evaluated long-term reliability of early glucometabolic classification of patients with AMI by repeated oral glucose tolerance tests (OGTTs).

RESEARCH DESIGN AND METHODS — A glucometabolic OGTT-based classification was obtained in 122 patients by measuring capillary whole-blood glucose. The classification was performed on three occasions, before hospital discharge and 3 and 12 months thereafter.

RESULTS — At discharge, 34, 31, and 34% were classified as having normal glucose tolerance, impaired glucose tolerance (IGT), or type 2 diabetes, respectively, and 93% of all patients with type 2 diabetes were still classified with type 2 diabetes ($n = 27$) or IGT ($n = 12$) after 12 months. The agreements between the OGTTs at discharge and 3 and 12 months were $\kappa = 0.35$, $P < 0.001$, and $\kappa = 0.43$, $P < 0.001$, respectively.

CONCLUSIONS — The outcome of an OGTT performed in AMI patients at hospital discharge reliably informs on long-term glucometabolic state.

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In recent years, focus has been devoted to the high prevalence of previously undiagnosed glucose abnormalities in patients with acute myocardial infarctions (AMIs) as reported by the GAMI (Glucose tolerance in Acute Myocardial Infarction [1]) Study and subsequently confirmed by the Euro and China Heart Surveys (2,3). These findings attracted further attention when it recently became evident that postinfarction patients with newly detected disturbed glucose metabolism are at an increased risk for cardiovascular morbidity and mortality (4,5), emphasizing the importance of diagnosing these patients at an early stage.

Classification of glucose abnormalities should, according to the World Health Organization (WHO) (6), be based on fasting and postload plasma glucose obtained by a standardized oral glucose tolerance test (OGTT), while the most recent American Diabetes Association (ADA) criteria (7) includes fasting blood glucose only. The latter method will, however, identify only about one-third of individuals defined with newly detected diabetes by means of an OGTT (1,8,9).

This analysis from the GAMI Study aimed at investigating the long-term reliability of early classification of glucose abnormalities using OGTT in patients with AMI without previously known type 2 diabetes.

RESEARCH DESIGN AND METHODS

A detailed description of the GAMI Study has been presented elsewhere (1). The inclusion criteria were suspected AMI, no previously known diabetes, baseline capillary blood glucose <11.1 mmol/l, serum creatinine <200 μmol/l, and age ≤80 years. A total of 181 participants were enrolled, of whom 168 were characterized on discharge after an OGTT as having normal glucose tolerance (NGT), impaired glucose tolerance (IGT), or type 2 diabetes. The present report is based on the 122 patients, who at all occasions during follow-up (discharge and 3 and 12 months) could be reclassified into the three groups.

A standardized OGTT (75-g glucose in 200 ml water) was performed at hospital discharge (day 4 or 5) and at 3 and 12 months. Blood glucose was analyzed immediately in capillary whole blood by means of the HemoCue procedure (photometer; HemoCue, Ángelholm, Sweden). A detailed description of laboratory methods has been presented elsewhere (1,10). Homeostasis model assessment of insulin resistance (HOMA-IR) was calculated in fasting condition according to Matthews et al. (11). Adjusted insulinogenic index (IGI) was calculated as $(\Delta I_{30}/\Delta G_{30})$/HOMA-IR (12). Type 2 diabetes and IGT were defined according to the WHO definition (6), and AMI was defined according to criteria recommended

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Abbreviations: ADA, American Diabetes Association; AMI, acute myocardial infarction; EASD, European Association for the Study of Diabetes; ESC, European Society of Cardiology; GAMI, Glucose tolerance in Acute Myocardial Infarction; HOMA-IR, homeostasis model assessment of insulin resistance; IGI, insulinogenic index; IGT, impaired glucose tolerance; NGT, normal glucose tolerance; OGTT, oral glucose tolerance test; WHO, World Health Organization.

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

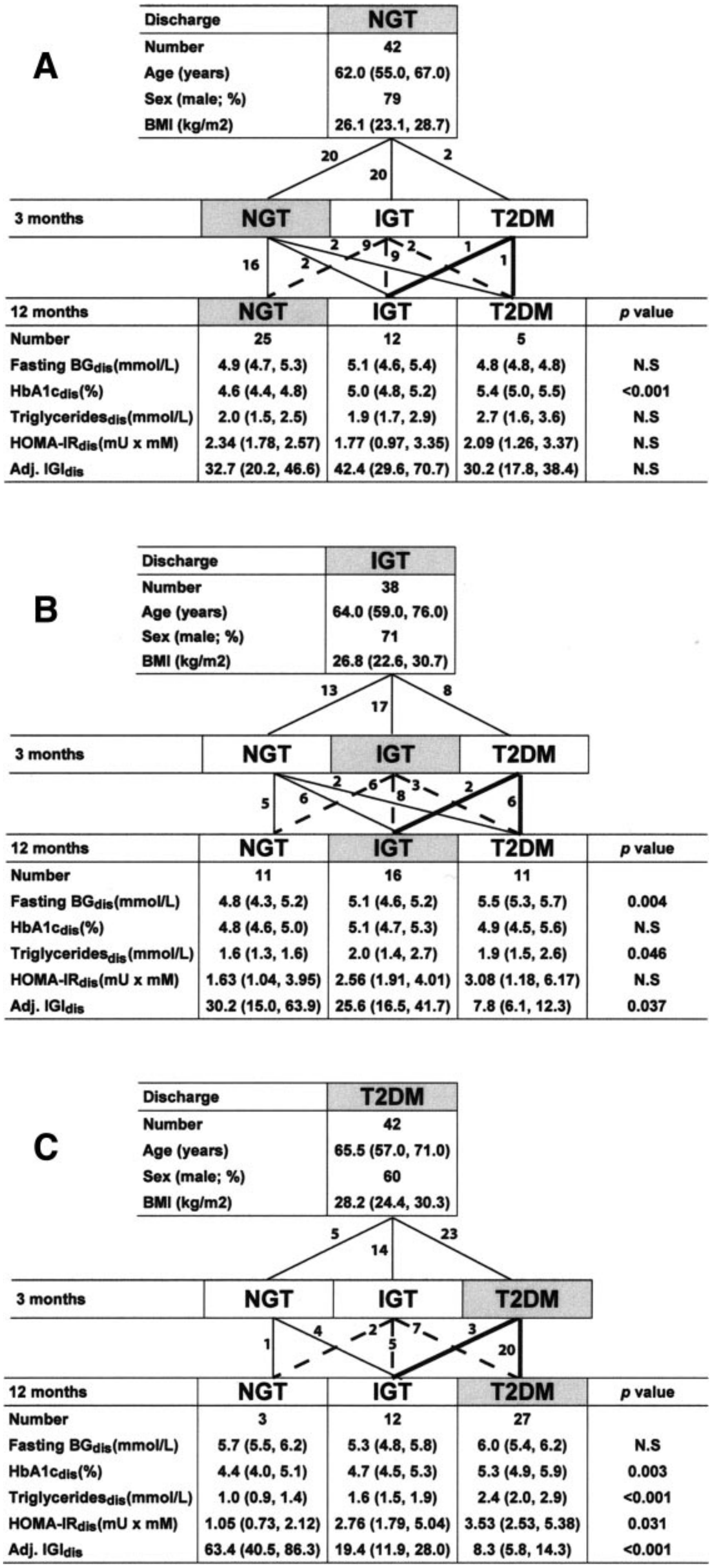

Figure 1—*Patients with NGT (*A*), IGT (*B*), and type 2 diabetes (*C*) at hospital discharge. Biochemical variables are all from hospital discharge and are presented as median (lower quartile, upper quartile).* P *value is based on Jonckheere-Terpstra's test. Adj. IGI, adjusted IGI [(ΔI_{30}/ΔG_{30})/HOMA-IR]; BG, blood glucose; T2DM, type 2 diabetes.*

by the European Society of Cardiology (ESC) and the American College of Cardiology (13). Concordance rates between OGTTs performed at different occasions were calculated as weighted Cohen's κ, where in case of complete agreement $\kappa = 1$; in case of no agreement (other than what would be expected by chance) $\kappa = 0$ (14). A two-sided P value <0.05 was regarded as statistically significant. All analyses were made using SAS version 9.1.3 (SAS Institute).

RESULTS

Glucose tolerance groups during follow-up

The OGTT-based glucometabolic classification at the time for hospital discharge revealed that 34% of the 122 patients had NGT, while 31 and 34% were classified as having IGT or type 2 diabetes, respectively.

A comparison between the OGTT-based glucometabolic classifications performed at discharge and after 3 and 12 months is presented in Fig. 1. There were no significant differences in baseline age, sex, or BMI between the three glucose tolerance groups (Fig. 1). The concordance between the OGTTs at discharge (DIS) and 3 and 12 months (3M and 12M, respectively) according to weighted κ statistics were DIS-3M $\kappa = 0.35$, $P < 0.001$; DIS-12M $\kappa = 0.43$, $P < 0.001$; and 3M-12M $\kappa = 0.48$, $P < 0.001$.

Biochemical characteristics at discharge

Patients changing from NGT at discharge to IGT or type 2 diabetes at 12 months had significantly higher levels of A1C at discharge (Fig. 1*A*), and those with IGT at discharge who changed to type 2 diabetes during follow-up had significantly higher levels of fasting blood glucose and triglycerides and lower adjusted IGI (Fig. 1*B*). Patients originally classified with type 2 diabetes and remaining in this group had higher discharge levels of A1C, triglycerides, and HOMA-IR and lower adjusted IGI (Fig. 1*C*). There were no significant differences in BMI between the different glucose tolerance groups at any occasion.

CONCLUSIONS— This study reveals that glucometabolic classification based on an OGTT at hospital discharge in patients with AMI is reliable, thereby contributing to the early detection of patients in need for special attention.

Of all AMI patients diagnosed with type 2 diabetes after an OGTT at discharge, 93% were still classified as such (64%) or as having IGT (29%) after 12 months. In the same manner, 60% of the patients classified with NGT at discharge remained normal after 12 months, although 12% had developed type 2 diabetes.

Patients with type 2 diabetes both at discharge and after 12 months had a more diabetic phenotype at discharge with increased A1C, triglycerides, and HOMA-IR and decreased β-cell secretion measured as adjusted IGI. Thus, an evaluation of the complete glucometabolic profile can provide additional information in patients with borderline OGTT results justifying future reevaluation.

In the recently published ESC/European Association for the Study of Diabetes (EASD) guidelines on diabetes, pre-diabetes, and cardiovascular disease (15), patients without known diabetes but with established cardiovascular disease are recommended to be investigated with an OGTT—a test still not recommended in routine practice by the ADA (7). To increase the likelihood of detecting patients with IGT by the use of fasting glucose only, ADA recently lowered the threshold for impaired fasting plasma glucose to 5.6 mmol/l. A recent report showed that even if the concordance between the WHO and the ADA criteria increased with this lower cutoff, 29% of patients with diabetes revealed by an OGTT and 57% with IGT would still have remained undiagnosed using fasting plasma glucose (9). Our data were based on bedside monitoring with capillary whole blood by the HemoCue procedure (1). A more common approach is to use venous plasma glucose measurements.

In conclusion, this study shows that the outcome of an OGTT before hospital discharge in patients with AMI is indeed a reliable measure of the glucometabolic state. We recommend that an OGTT is performed on all AMI patients already at hospital discharge, followed by early initiation of a management strategy according to recently published ESC/EASD guidelines (15).

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