Key Global Literature

Vivian Fonseca, MD
From the Division of Endocrinology, Tulane University Medical Center, New Orleans, Louisiana. E-mail: vfonseca@tulane.edu.

Szabo Z, Arnqvist H, Hakanson E, Jorfeldt L, Svedjeholm R: Effects of high-dose glucose-insulin-potassium on myocardial metabolism after coronary surgery in patients with type II diabetes. *Clin Sci* 101:37–43, 2001

Findings. Szabo et al. investigated the use of a glucose-insulin-potassium infusion (GIK) on myocardial substrate utilization after coronary surgery in 20 patients with type 2 diabetes. Patients were randomly allocated to either postoperative high-dose GIK or standard postoperative care, including insulin infusion, if necessary, to keep blood glucose <10 mmol/l. Myocardial substrate utilization and hemodynamic status were studied using coronary sinus catheters and Swan-Ganz catheters, respectively. Infusion of GIK caused a shift toward carbohydrate utilization, with significant lactate uptake throughout the study period and significant uptake of glucose after 4 h. Arterial levels of nonesterified fatty acids and β-hydroxybutyric acid decreased, and after 1 h no significant uptake of these substrates was found. Increases in the cardiac index and stroke volume index were found in patients treated with GIK.

Significance. The DIGAMI study clearly established the value of insulin infusions for patients with diabetes presenting with a myocardial infarction. Good diabetic control perioperatively has also been shown to be useful in diabetic subjects undergoing a variety of surgical procedures, including cardiac surgery. The effects of GIK on cardiac metabolism have been studied previously in nondiabetic patients after cardiac surgery. Although patients with diabetes can be expected to benefit most from such treatment, the impact of GIK in diabetic patients undergoing cardiac surgery has not been unexplored. The authors conclude that high-dose GIK can be used in diabetic patients after cardiac surgery to promote carbohydrate uptake at the expense of nonesterified fatty acids and β-hydroxybutyric acid.

Clinical Impact. This study adds scientific support to the recommendation of using insulin infusions along with adequate nutrition (glucose) and electrolytes. Perhaps it will help us convince our colleagues in cardiology and surgery to use in hospital intensive therapy for diabetic patients.

Taverna MJ, Pacher N, Bruzzo F, Slama G, Selam JL: Beta-cell function evaluated by HOMA as a predictor of secondary sulphonylurea failure in type 2 diabetes. *Diabet Med* 18:584–588, 2001

Findings. The goal of this study was to evaluate if the homeostasis model assessment (HOMA) model utilizing a corrected fasting plasma insulin and glucose ratio allowed a simple evaluation of residual insulin secretion and sensitivity and was therefore a better predictor of the insulin-requiring stage of type 2 diabetes than clinical indices. HOMA was measured in 84 type 2 diabetic patients aged 58 ± 6 years, with a history of diabetes for 11 ± 4 years, who were resistant to maximal doses of sulphonylureas. Despite reinforced appropriate diet recommendations, 62 of these patients remained hyperglycemic (insulin-requiring group). Potential predictors of insulin-requiring status in these patients were compared with those in patients who did not require insulin. Age, duration of diabetes, BMI, and HOMA value for insulin sensitivity (71 ± 6 vs. 76 ± 7%, normal values 59–161%) were comparable in the two groups. HbA_{1c} was higher (10.0 ± 0.2 vs. 8.3 ± 0.3%, $P < 0.001$) and HOMA insulin secretion values were lower (25 ± 2 vs. 43 ± 6%, normal values 70–150%, $P < 0.01$) in the insulin-requiring group. Of the following potential predictors, HbA_{1c} >8%, duration of diabetes ≥10 years, HbA_{1c} combined with diabetes duration, insulin sensitivity ≤40%, and insulin secretion ≤20%, the latter showed the best positive predictivity (86% with low insulin secretion were insulin-requiring patients).

Significance. Secondary failure to oral hypoglycemic agents is a common stage in the natural history of long-standing type 2 diabetes, and it is usually assessed by nonstandardized indices requiring clinical assessment, including hyperglycemia resistant to maximum doses of sulphonylureas despite appropriate diet. The study demonstrates that *1*) HOMA is a simple and good predictor of the insulin-requiring stage in type 2 diabetes, and *2*) this stage of diabetes is characterized by a further decline of insulin secretion rather than of insulin sensitivity.

Clinical Impact. A test that provides an objective indication that a patient does need insulin seems attractive. It may help convince patients that they must start insulin soon. However, these findings need to be validated before this test can be used in clinical practice.

Jones SC, Bowes PD, Hall E, Connolly V, Kelly WF, Bilous RW: HOPE for patients with type 2 diabetes: an application of the findings of the MICRO-HOPE substudy in a British hospital diabetes clinic. *Diabet Med* 18:667–670, 2001

Findings. Jones et al. have analyzed data on people ($n = 1,370$) with type 2 diabetes without proteinuria to determine whether they met inclusion criteria of the MICRO-HOPE substudy of the HOPE study. They assumed that such patients could anticipate

reductions in cardiovascular events with ramipril or other ACE inhibitor treatment. Of nonproteinuric people with type 2 diabetes, 78% had at least one additional cardiovascular risk factor and would thus have met inclusion criteria of the MICRO-HOPE substudy, and 29% were already taking an ACE inhibitor. The remaining 764 patients were similar to ramipril-treated participants in the MICRO-HOPE substudy. Treatment with ramipril for 4.5 years would be anticipated to reduce cardiovascular deaths by 26, revascularization procedures by 19, and admissions for myocardial infarction and stroke by 18 and 26, respectively.

Significance. A large proportion of nonproteinuric people with type 2 diabetes (78%) have additional cardiovascular risk factors. Only a small proportion of these "high-risk" people currently receive treatment with an ACE inhibitor. The incidence of cardiovascular events could be reduced if more patients were treated with ramipril and if other cardiovascular risk factors were addressed.

Impact. Studies like this demonstrate the clinical (and indirectly the economic) impact of physicians not translating the results of major clinical trials into practice. Hopefully, awareness of this problem will lead to greater use of strategies to reduce cardiovascular risk, when clinically indicated.

Juneja R, Hirsch IB, Naik RG, Brooks-Worrell BM, Greenbaum CJ, Palmer JP: Islet cell antibodies and glutamic acid decarboxylase antibodies, but not the clinical phenotype, help to identify type 1(1/2) diabetes in patients presenting with type 2 diabetes. *Metabolism* 50:1008–1013, 2001

Findings. In this study, 125 patients, recently diagnosed clinically with type 2 diabetes (age ≥30 years, no history of ketonuria or ketoacidosis, and not requiring insulin treatment) were tested for the presence of several antibodies (Ab) implicated in the pathogenesis of type 1 diabetes: islet cell antibodies (ICA), insulin autoantibodies (IAA), and antibodies to GAD (GADAb) and IA-2A (IA-2Ab). Of these patients, 36 (29%) were positive for at least one antibody; 32 (26%) were ICA positive and 20 (16%) were GADAb positive. Insulin autoantibodies and IA-2Ab occurred less frequently in 2 (1.6%) and 8 (6.4%) patients, respectively. There was no significant difference in the ages at diagnosis between the Ab-positive and Ab-negative patients. Ab-positive patients were less obese (BMI 28.3 vs. 32.0 kg/m^2, respectively). Clinical presentation with symptomatic diabetes was more common in Ab-positive patients, whereas in Ab-negative patients, diagnosis was more often incidental. However, >95% of patients overlapped in both age and BMI, irrespective of antibody status. Similarly, 42% of Ab-positive patients had their diabetes diagnosed incidentally, whereas 29% of Ab-negative patients presented with polyuria and polydipsia.

Significance. There is increasing recognition that the late-onset autoimmune diabetes (LADA, or "type 1½ diabetes") is fairly common. This study confirms that making a diagnosis on clinical grounds is fraught with difficulty due to overlap in clinical presentation between Ab-positive and -negative patients. This study concludes that screening with antibodies, mainly ICA and GAD, and not with age, BMI, or clinical presentation, should be used to identify type 1½ diabetes.

Clinical Impact. The finding of this study greatly supports the use of Ab tests in clinical practice, thus supporting an emerging trend for carrying such tests. However, before they are widely recommended, these tests should be validated in a variety of populations/ethnic groups, and the cost effectiveness of the procedures should be investigated.

Cosway R, Strachan MW, Dougall A, Frier BM, Deary IJ: Cognitive function and information processing in type 2 diabetes. *Diabet Med* 18:803–810, 2001

Findings. Cosway et al. assessed cognitive function and information-processing ability in 38 patients with uncomplicated type 2 diabetes and 38 nondiabetic control subjects. The two groups were matched for age, premorbid intellectual ability, and other medical disorders. They administered a battery of tests that assessed different levels and domains of cognitive functions, including verbal and visual memory, executive function, general mental ability, and efficiency of information processing. There were no significant differences between the diabetic and control groups on any measure of cognitive function or information processing. However, there was a significant association between duration of diabetes and poorer performance on several measures of verbal memory.

Significance. Is type 2 diabetes associated with impairment of cognitive function independent of glycemic control and comorbid conditions? This study suggests that type 2 diabetes of long duration is associated with a decline in cognitive function, but other diabetes-related factors, such as macrovascular disease, hypertension, and depression, may also contribute.

Clinical Impact. These preliminary data were obtained from a small population sample. If confirmed, however, it suggests that we may need to reconsider patient education strategies and methods to improve treatment compliance in patients with long-standing diabetes.