Augmented metabolic control improves myocardial diastolic function and perfusion in patients with non-insulin dependent diabetes

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Diastolic dysfunction and compromised myocardial blood flow are characteristic findings in patients with non-insulin dependent diabetes. We conducted a pilot trial to test the hypothesis that intensified metabolic control would improve myocardial function and perfusion in patients with non-insulin dependent diabetes.

DESIGN AND METHODS
Twenty five patients with non-insulin dependent diabetes (19 men, mean age 60 (9) years, diabetes duration 8 (7) years) were subjected to intensified metabolic control based on an increased dose of insulin (group A: n = 16, fasting β glucose 11 (4) mmol/l) or of oral treatment (group B: n = 9, fasting β glucose 11 (3) mmol/l). Exclusion criteria were a moderate to severe degree of diabetic microvascular complications, clinical signs of heart failure, valvar disease, severe hypertension, and concomitant hepatic or renal dysfunction. A further eight patients were studied as controls during unchanged medication (mean age 62 (6) years, fasting β glucose 8 (2) mmol/l).

Evidence of coronary artery disease was assessed based on coronary angiography or stress echocardiograms (dobutamine 10–40 mg/kg/min). All patients were trained to measure blood glucose with a reflectometer (Accutrend Sensor, Roche Diagnostics, Stockholm, Sweden). Self reported concentrations of fasting blood glucose averaged from three days before each visit served as a reference for glucose control. Myocardial perfusion and function were assessed by ultrasound technology at rest and during maximum vasodilatation (dipyridamole 0.84 mg/kg) before (visit 1) and three weeks after (visit 2) modification of antidiabetic treatment.

RESULTS
Baseline characteristics as regards diabetes and its complications were comparable between the two groups and so were additional risk factors for cardiovascular disease such as hypertension (63%), hyperlipidaemia (54%), and smoking (21%). At visit 1, the antidiabetic treatment was similarly
glucose \( (r = 0.52, p < 0.002) \) both in patients with and in patients without evidence for coronary artery disease (fig 2). In the controls, all parameters remained unchanged.

**DISCUSSION**

The noted effect of augmented diastolic function correlated with improved glycaemic control both in patients with and in patients without evidence of ischaemic heart disease. Although the exact pathophysiological mechanisms remain unknown, improved myocardial energy substrate utilisation is likely to be involved. Another potential mechanism is augmented microvascular perfusion. Endothelial dysfunction is aggravated by hyperglycaemia and may be partially reversed by insulin. Regulation of recruitable capillaries is influenced by hyperglycaemia and by insulin. A reasonable assumption is that effects on endothelial function are involved as shown by forearm blood flow with intensive insulin based treatment in patients with non-insulin dependent diabetes and by the present study for the first time in the myocardium as well.

This pilot investigation has the disadvantage related to observational studies of patients who were recruited from clinical practice with intensified antidiabetic treatment based on clinical needs. Such a study design may cause selection bias but has provided a possibility for initial testing of the hypothesis that insulin based metabolic control would exert beneficial effects.

The findings in this study are new and warrant confirmation in future randomised trials. From the present observations it is reasonable to assume that normoglycaemia and insulin improve myocardial diastolic function and perfusion in non-insulin dependent diabetes. Moreover, the findings support the hypothesis that cardiac abnormalities reported in diabetes mellitus contain a component of reversibility. Taken together this may have important future treatment implications.

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