AIMS: To evaluate effects of the oral antidiabetic insulinotropic agent nateglinide on myocardial blood flow (MBF) and microvascular reactivity in Type 2 diabetic patients. METHODS: Forty-seven Type 2 diabetic patients were randomly assigned 2:1 to nateglinide 120 mg (t.i.d., n = 33) or placebo (n = 14). At baseline and after 16 weeks of treatment, MBF was quantified using positron emission tomography with N-13 ammonia at rest, during endothelial-dependent stimulation by cold pressor test and during adenosine-mediated vasodilation. Additional blood samples were taken to assess glycaemic control and lipid profile. RESULTS: MBF at rest and during adenosine did not change during the study. The percentage of flow increase from rest during cold pressor test did not improve significantly in the nateglinide group vs. placebo (from 26.1 +/- 37.2% to 29.1 +/- 27.8% between week 0 to week 16 for nateglinide vs. 14.9 +/- 37.1% to 18.1 +/- 28.4% for placebo; P = 0.07 for nateglinide when adjusted for higher baseline values). Nateglinide decreased HbA1c by 0.4% (from 7.6 +/- 0.9% to 7.2 +/- 1.3%) compared to an increase of 0.5% in the placebo group (from 7.9 +/- 0.8% to 8.4 +/- 1.7%; P = 0.02 for nateglinide). No differences between the two groups were observed in insulin levels and lipid status. CONCLUSIONS: Nateglinide neither improved, nor impaired myocardial
blood flow in Type 2 diabetic patients. Potential effects on endothelial-dependent myocardial blood flow remain to be investigated further. Positron emission tomography is a sensitive approach to assess the effects of therapeutic agents on myocardial blood flow in patients with diabetes.