During the past decades, significant strides in the treatment and management of diabetes mellitus have been made, especially with regard to the multifactorial approach in management. It is common knowledge that diabetes imposes a significant risk for both micro- and macrovascular complications. Microvascular disease can be prevented by strict glycaemic control, as proven in the Diabetes Control and Complications Trial (DCCT)\(^1\) and the United Kingdom Prospective Diabetes Study (UKPDS).\(^2\) Sadly, the association between strict glycaemic control and macrovascular disease was not as clear as that for microvascular disease.

Cardiovascular disease, however, remains a major cause of death and morbidity in diabetic patients.\(^3\) The association between diabetes and macrovascular disease is so strong that it was considered a myocardial infarction equivalent after the Multiple Risk Factor Intervention Trial (MRFIT).\(^4\) The question why glycaemic control did not significantly improve cardiovascular risk (coronary heart disease, stroke and peripheral vascular disease) was still unanswered. The possible reasons for this were thought to be, firstly, as a result of too short follow up (DCCT: mean 6.5 years and UKPDS: 8 years) and, secondly, because the aim of these studies was to improve glycaemic control, as measured by fasting blood glucose and Hb\(A_1c\). Both these parameters are crude indicators of glycaemic control since it does not fully account for short-term glycaemic excursions.

The first concern was resolved in type 1 diabetic patients with the Epidemiology of Diabetes Interventions and Complications (EDIC) study. The EDIC study was an 11-year follow up of the DCCT study subjects. It demonstrated a 3% absolute reduction in cardiovascular risk, despite the fact that the difference in glycaemic control between the original intensive and conservative treatment groups declined significantly after the DCCT study ended.\(^5\)

The second issue of short-term glycaemic control, especially related to post-meal hyperglycaemia, came under more careful scrutiny after a number of epidemiological studies. These included the Hoorn study,\(^6\) the Honolulu Heart study\(^7\) and more recently the Diabetes Epidemiology Collaborative Analysis of Diagnostic Criteria (DECODE) study.\(^8\) They all demonstrated that the risk for cardiovascular mortality is more strongly associated with the two-hour post-oral glucose tolerance values rather than with fasting plasma glucose levels. This is also the case in non-diabetic patients with an elevated two-hour plasma glucose value.\(^8\) The assumption that the two-hour blood glucose level, as part of an oral glucose tolerance test (OGTT), can be extrapolated to the two-hour post-prandial blood glucose value seems to be valid, since a good correlation exists between the two-hour blood glucose level after a standardised meal and an OGTT.\(^10\)

Circumstantial evidence also exists to imply harmful effects of post-meal hyperglycaemia and an increased risk of cardiovascular disease. These studies make use of surrogate markers, such as carotid intima–media thickness,\(^11\) endothelial dysfunction,\(^12\) oxidative stress\(^13\) and inflammation\(^14\) as indicators of increased risk.

The evidence suggests that post-meal hyperglycaemia imposes an increased cardiovascular risk, but does the treatment of hyperglycaemia in the post-meal period improve this risk? A number of studies are currently available to confirm this in type 2 diabetic patients. These studies indicate significant advantages for the use of drugs that specifically target post-meal hyperglycaemia, such as meglitinides\(^15\) and
alpha-glycosidase inhibitors.\textsuperscript{16}

With regard to insulin regimens that specifically target post-meal hyperglycaemia, no completed study is available to demonstrate a reduction in cardiovascular risk. Ample evidence is, however, available to demonstrate the efficacy of insulin, especially the insulin analogues, in lowering the post-meal glucose, and thereby mimicking the normal pattern of insulin secretion more closely.\textsuperscript{11} Dietary changes aiming to decrease the glycaemic index and glycaemic load, which lower post-prandial glucose excursions, also seem to reduce the risk of cardiovascular disease.\textsuperscript{17}

Against this background, the International Diabetes Federation (IDF) produced guidelines for the management of post-meal glucose, which advise control of blood glucose, not targeting fasting and HbA\textsubscript{1c}, values only, but with the specific aim of controlling post-meal blood glucose. The target stated for two-hour post-meal blood glucose is 7.8 mmol/l. This requires frequent blood glucose monitoring, low glycaemic index meal plans, use of post-prandial glucose regulators as well as the early use of insulin in patients with type 2 diabetes. For type 1 diabetic patients, a more refined insulin regimen that mimics normal insulin secretion, and frequent post-prandial blood glucose measurements is necessary to achieve this target.

Currently, the treatment of hyperglycaemia consists of three aspects that need to be fulfilled before a patient can be considered well controlled: HbA\textsubscript{1c}, less than 6.5\%, fasting blood glucose less than 5.5 mmol/l and now also post-meal blood glucose less than 7.8 mmol/l. With these aspects addressed, other risk factors should not be forgotten, since diabetes remains a multifactorial disease with more than just blood glucose that needs to be controlled.

References