

## 糖尿大血管與小血管併發症處置新知介紹

林時逸

台中榮總新陳代謝科

The diabetic chronic complications are a big burden for health systems, and more than half of diabetes related costs is used to treat vascular complications. Chronic hyperglycemia in association with the other several metabolic perturbations in diabetes, including dyslipidemia, hyperinsulinemia and hypertension, can activate several pathways and result in activation of pro-inflammatory and profibrotic cytokines, and finally pathological and clinical vascular abnormalities in diabetes.

### **Glycemic goals and complications in diabetes**

In newly diagnosed type 2 diabetes in UKPDS, it is demonstrated that intensive glycemic control (mean A1C 7%) was associated with significantly decreased microvascular complications, and the benefit of strict glycemic control can be prolonged in the long-term follow-up. In type 1 diabetes, the DCCT shows that improved glycemic control is associated with significantly decreased rates of retinopathy, nephropathy and neuropathic complications, and the EDIC study demonstrates that there is a persistent benefit. In type 2 diabetes with longer disease duration (8-11 yrs), 3 trials (ACCORD, ADNANCE, VADT) show that lower A1C levels (median A<sub>1c</sub> 6.4–6.9% in the intensive arms compared with 7.0–8.4% in the standard controls) were associated with reduced onset or progression of microvascular complications.

Patients with type 2 diabetes have an increased risk of cardiovascular events. In type 2 diabetes in UKPDS, intensive treatment in newly diagnosed patients may marginally reduce CVD rates, and after 10 years of follow-up, those with intensive glycemic control had significant long-term reductions in MI and all-cause mortality. However, in the ACCORD, ADVANCE, and VADT studies, it is found that there was no significant reduction in CVD outcomes with intensive glycemic control.

### **Blood pressure and lipid goals and diabetic complications**

Hypertension is a major risk factor for both macrovascular and microvascular complications. Randomized clinical trials have demonstrated the benefit of lowering blood pressure to 140 mmHg systolic and 90 mmHg diastolic in diabetic individuals with reduction of cardiovascular events, stroke, and diabetic kidney disease. Meta-analysis of randomized trials of adults with type 2 diabetes comparing intensive blood pressure targets with upper limit of 130 mmHg systolic and 80 mmHg diastolic to standard targets of upper limit of 140–160 mmHg systolic and 85–100 mmHg diastolic found no significant reduction in mortality or nonfatal myocardial infarction. However, there was a statistically significant 35% relative risk reduction in stroke.

Patients with type 2 diabetes have an increased prevalence of lipid abnormalities, contributing to their high risk of cardiovascular disease in diabetes. Meta-analyses in

diabetes from 14 randomized trials of statin therapy demonstrate a 9% reduction in all-cause mortality and 13% reduction in vascular mortality for each mmol/L (=38mg/dl) reduction in LDL cholesterol. However, most statins trials only evaluated specific doses of statins but no aiming for specific LDL cholesterol goals. In light of this fact, the 2015 ADA Standards of Care have been revised to recommend when to initiate and intensify statin therapy based on risk profile. For patients of all ages with diabetes and overt CVD, high-intensity statin therapy should be added. In patients with diabetes aged less than 40 years with additional CVD risk factors or, moderate or high-intensity statin and lifestyle should be considered, and in patients with diabetes aged 40– 75 years with additional CVD risk factors, high-intensity statin should be used. For patients with diabetes aged greater than 75 years without additional CVD risk factors, consider using moderate-intensity statin therapy and lifestyle therapy is suggested. For patients with diabetes aged greater than 75 years with additional CVD risk factors, moderate- or high-intensity statin therapy and lifestyle therapy should be considered. In the DAROC Clinical Practice Guidelines for Diabetes Care- 2015, it is suggested that treatment goals for blood pressure (BP) control (i) for people with diabetes and hypertension is <140/90 mmHg (ii) lower BP targets (such as <130/80 mmHg) may be appropriate for individuals with diabetic nephropathy (iii) for diabetic patients over 65 years old, a less stringent BP goal may be considered, such as <150/90 mmHg. For the blood lipid treatment goal, LDL-cholesterol is the primary target and should be less than 100mg/dL (less than 70 mg/dL in patients with cardiovascular disease). Non-HDL-cholesterol is the secondary target and should be less than 130mg/dL (less than 100 mg/dL in patients with cardiovascular disease).

### **Conclusion**

Glucose, blood pressure and cholesterol control are a major focus in the management of patients with type 2 diabetes. A comprehensive program for cardiovascular risk factor reduction program with adoption of healthy lifestyle is necessary. The clinical team should also encourage patient adherence to therapy through education and try to optimize care.