

## **Diabetes and Thrombosis**

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The ongoing epidemics of obesity and type 2 diabetes are causing major increases in the number of diabetic patients, now reaching approximately 8% of the entire US population, and more than 20% of adults age 60 or older. This large number of patients has been shown to be at high risk for the development of thrombotic disease, including coronary artery disease, cerebrovascular disease and peripheral vascular disease.

High glucose levels are tightly correlated with increased risk of cardiovascular disease (CVD) starting in the normal range, then progressing to different states of impaired glucose tolerance and eventually overt diabetes. CVD is not only more prevalent in diabetic patients, but also has worse outcomes, with higher morbidity as well as mortality. While the reasons for these associations are not completely clear, the diabetes state is associated with thrombotic events in both the large and small vasculature and several potential mediators have been described in animal models of diabetes as well as in diabetic patients, including abnormalities in the vascular endothelium, in fibrinolysis, coagulation and platelet hyperreactivity.

While it is established that increased glucose levels are linked to increased CVD, it is not clear what is the role of treating hyperglycemia in the prevention or treatment of CVD. Several large clinical studies, in both type 1 and type 2 diabetic patients, have definitely shown an association between tight glycemic control and reduced microvascular disease, but the picture with CVD is more complex. The effects of tight glucose control on CVD disease take a much longer time to be manifest and they also differ depending on the patient population. Recently diagnosed patients, with lower risk of CVD show a beneficial effect of tight glucose control in the prevention of CVD, however, older, higher risk patients have not found to benefit from tight glucose control in term of decreased CVD burden, and in one study an increase of sudden death was observed in more tightly controlled type 2 diabetic patients. A more systematic approach, addressing multiple CVD risk factors, including glycemic control, blood pressure and lipid control has been shown to reduce CVD by > 50%, however we are still far from achieving these goals in the large majority of diabetic patients.