Effects of glycemic control and other determinants on vascular disease in type 2 diabetes

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Abstract

Cardiovascular disease is the leading cause of death in patients with type 2 diabetes, with more than 77,000 deaths each year. The risk remains high despite normalization of well-known cardiovascular risk factors, and the impact of glycemic control on risk reduction remains controversial. Deleterious changes in fibrinolysis, platelet function, and coagulation secondary to insulin resistance and/or the metabolic derangements of type 2 diabetes have emerged as likely mechanisms underlying increased cardiovascular risk. Plasminogen activator inhibitor–1 (PAI-1) is an inhibitor of the fibrinolytic system. Thus, elevated concentrations of PAI-1 promote persistence of clots. Concentrations of PAI-1 are elevated in the blood and vessel walls of patients with type 2 diabetes or other insulin-resistant states. We have hypothesized that increased PAI-1 can create conditions favorable to the evolution of unstable, lipid-laden atherosclerotic coronary plaques, thereby rendering patients with diabetes highly susceptible to rupture of vulnerable plaques and acute coronary syndromes. Therapeutic interventions that may alter this evolution by reducing concentrations of PAI-1 or correct metabolic derangements that promote it are being studied. Antiplatelet therapy has been directed at the increased platelet reactivity characteristic of patients with diabetes. Its use has reduced complications after percutaneous coronary intervention following the onset of unstable angina. Amelioration of diabetic cardiomyopathy by correction of impaired myocardial energy metabolism and limiting the accumulation of advanced glycation end products is being evaluated as well.