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Editorial

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The Challenge of Dysglycemia and Coronary Heart Disease

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The prevalence of type 2 diabetes mellitus (T2DM) is increasing globally, and although there is a small increase in the incidence of type 1 diabetes mellitus, T2DM accounts for 95% of all individuals with diabetes.[1] A high prevalence of undiagnosed glucose abnormalities has been demonstrated in patients with acute coronary syndrome (ACS) including acute myocardial infarction (AMI),[2] and several studies have shown that newly detected glucose metabolism abnormalities in the form of impaired glucose tolerance and diabetes represent an independent risk for cardiovascular mortality and morbidity.[3,4] There seems to be a curvilinear relation between post-oral glucose tolerance test, glucose levels and the risk for cardiovascular disease, and the risk increases already in the non-diabetic range of glucose levels.

There are several mechanisms linking diabetes to an increased risk of cardiovascular disease. Patients with T2DM are prone to atherothrombosis, which increases the risk of cardiovascular events and mortality. Apart from classical risk factors for atherosclerosis such as hypertension and dyslipidemia, which co-exist in many patients with T2DM, the increased atherothrombotic risk is also explained by a pro-inflammatory state, which is partly due to endothelial and smooth muscle cell dysfunction.[5] Another important factor contributing to the increased risk of coronary events in patients with T2DM is dysregulation of factors involved in coagulation and platelet activation.[6]

Acute ST-elevation myocardial infarction (STEMI) accounts for approximately 30-40% of patients with ACS. In patients with STEMI, peak glycaemia has been found to be an independent predictor of in-hospital mortality.[7,8] Presence of diabetes is also an independent predictor of incomplete ST-segment recovery, which is used to quantify myocardial microvascular dysfunction and is a powerful predictor of long-term mortality in patients undergoing primary percutaneous coronary intervention (PPCI).[9] There is a strong association between T2DM and impaired myocardial perfusion after PPCI.[9-11] It has been demonstrated that despite a successful PPCI and adequate epicardial flow (TIMI 3 flow), suboptimal myocardial perfusion frequently occurs among diabetic patients.[12-14] Interestingly, diabetes is independently associated with 30-day reinfarction after successful PPCI for STEMI.[15-17] Of note, diabetes mellitus seems to abolish the beneficial effect of PPCI on the long-term risk of reinfarction compared with fibrinolysis.[18] Several mechanisms have been proposed to explain the independent association between hyperglycaemia and impaired myocardial microvascular function observed in patients undergoing PPCI. It has been suggested that hyperglycaemia may augment plugging of leukocytes in the capillaries as well as platelet activation and thrombus formation in the capillaries, increasing the risk of no-reflow after PPCI for STEMI. Vascular endothelial dysfunction, which is closely linked to impaired insulin sensitivity, has also been mentioned as a contributing factor to the no-reflow phenomenon. We have shown that microvascular reactivity is severely impaired in patients with diabetes and ACS, and that diabetes has a major influence on microvascular function in patients with coronary artery disease.[19] Strategies which help to restore microvascular endothelial function may thus improve diabetic control, as well as reduce microvascular complications such as myocardial microvascular dysfunction in ACS setting.

CONCLUSIONS

The prevalence of dysglycemia is high in patients with coronary heart disease, and it contrib-

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utes to increased risk for poor clinical outcome. In order to identify targets, modulation of which may improve cardiovascular prognosis in patients with dysglycaemia and ACS, the mechanisms of no-reflow after PPCI and their relationship with hyperglycaemia should be further investigated. Furthermore, new treatment strategies targeting myocardial perfusion after percutaneous coronary intervention and microvascular endothelial function are urgently needed.

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