Diabetes and cardiovascular disease

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Diabetes mellitus and obesity are major health concerns, and the worldwide incidence of these problems is growing at an alarming rate. This growth is disconcerting, because diabetes is associated with a high incidence of morbidity and mortality, and heart diseases are the major cause of death in the diabetic patient. This high risk for heart disease results from both a high incidence of coronary artery disease and hypertension in the diabetic, and the development of cardiomyopathies that occur independent of these risk factors. This leads to a high incidence of heart failure in the diabetic population. Although the mechanisms responsible for the high incidence of coronary artery disease and hypertension in patients with diabetes, insulin resistance, obesity, or combinations thereof, are reasonably well defined, the important mechanisms responsible for the non ischemic cardiac dysfunction induced in these individuals are less clear. It is well documented that diabetes can lead to a progressive cardiomyocyte dysfunction that can result in both diastolic and systolic dysfunction. A considerable research effort has focused on trying to understand what is responsible for the alterations in cardiomyocyte function in patients with diabetes.

Diabetes-induced alterations in cardiac energy metabolism are increasingly being recognized as important contributors to abnormal cardiac function in those with diabetes. High circulating concentrations of fatty acids in diabetes, and an increased reliance of the heart on fatty acids as a source of energy, not only inhibit myocardial glucose utilization, but also result in excessive accumulation of lipids in muscle. This lipid accumulation can further exacerbate insulin resistance in the heart muscle. High rates of fatty acid oxidation in the heart of the diabetic patient also contribute to the severity of ischemic injury, primarily by inhibiting glucose oxidation. Because of this, the aim of decreasing cardiac fatty acid metabolism is becoming an important therapeutic approach to the treatment of diabetes and its complications.

This issue of *Heart and Metabolism* addresses a number of key issues related to the effects of diabetes on cardiac function and cardiac metabolism. Articles by Sihem Boudina and by David Bell nicely define the cardiac clinical manifestations that occur in diabetes and insulin resistance, in addition to some of the potential therapeutic approaches to treating cardiac dysfunction in affected individuals. The article by Danielle Feuvray and that by Romain Harmancey and Heinrich Taegtmeyer define some of the energy metabolic changes that occur in diabetes that can lead to the development of cardiomyopathy and heart failure. Both articles highlight an excessive supply of fatty acid to the heart and the excessive use of fatty acids by the heart as potentially important factors contributing to the development of heart failure. This raises the possibility of altering fatty acid metabolism as an approach to treating diabetes-induced cardiac dysfunction. This can be achieved either by altering the supply of fatty acid to the heart or by directly modifying cardiac fatty acid oxidation. With regard to the latter, the article by Luis Rodríguez Padial describes some of the clinical benefit that can be achieved with trimetazidine, an inhibitor of fatty acid oxidation, in diabetic patients. It is interesting that this metabolic approach to the treatment of heart disease is particularly useful in the patient with diabetes, which may be attributable to the underlying metabolic abnormalities in fatty acid metabolism in this population of patients. G. Todiere and Mario Marzilli nicely describe some of the imaging approaches that can be used to assess the severity of metabolic abnormalities in diabetic individuals.

Editorial

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In addition to metabolic changes, abnormalities in the coronary microcirculation may also be an important contributor to the development of diabetic cardiomyopathy. To enable a better definition of this phenomenon, Maurizio Galderisi and Rosa Raia describe the usefulness of Doppler-derived coronary flow reserve measurements in assessing the severity of abnormalities of the coronary microcirculation.

The importance of diabetic cardiomyopathy in contributing to contractile dysfunction and heart failure in diabetes has now been well established. The importance of alterations in cardiac fatty acid metabolism in contributing to these cardiomyopathies is also becoming more evident. This raises the possibility that optimizing cardiac energy metabolism may become a more widely used therapeutic approach to treating heart failure in the diabetic.