



# Diabetes: getting to the heart of the matter

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The prevalence of diabetes worldwide has reached epidemic proportions, with the number of type 2 diabetes mellitus (T2DM) patients now exceeding 400 million.<sup>1</sup> This is a major concern, as T2DM patients are at a much higher risk of developing myocardial ischemia and heart failure than nondiabetic individuals.<sup>2</sup> As a result, cardiovascular disease is the major cause of death of T2DM patients.<sup>2</sup> Although initially considered a “vascular disease” with its associated accelerated atherosclerosis, it is now evident that diabetes also directly affects cardiac cellular mechanisms that can contribute to the incidence and severity of heart failure and ischemic heart disease. This creates both problems and opportunities when treating the diabetic patient with cardiovascular disease. The main problem is that the physician must not only treat the heart disease, but also control the diabetes. There is opportunity arising from understanding how diabetes directly affects the cellular mechanisms contributing to heart disease, as this has the potential to reveal new targets and approaches in treating cardiovascular disease in the diabetic. The articles in this issue of *Heart and Metabolism* address the important problem of cardiovascular disease in the diabetic while addressing both the causes and potential cures for cardiovascular disease in the T2DM patient.

The rapid rise in the incidence of T2DM worldwide is especially evident in the South Asian population where T2DM has increased dramatically in places such as India and China. In their article, Peter Nilsson and Louise Bennet highlight how diabetes is a global

concern and the importance of taking a global view in treating diabetes. They also discuss the significant issue of migration and T2DM risk, while emphasizing the importance of public measures to tackle the epidemic in migrant populations at risk for developing diabetes. This includes the promotion of healthy lifestyles and improvement of social conditions for these migrant populations.

The risk of developing heart failure positively correlates with the degree of hyperglycemia in the T2DM patient.<sup>3</sup> Although this would imply that lowering blood glucose should decrease cardiovascular risk, this is not always the case. Despite the rapidly expanding list of antihyperglycemic agents used to treat T2DM, many of these agents are not associated with improved cardiovascular outcomes. However, as reviewed by myself in this issue of *Heart and Metabolism*, recent large clinical outcome trials have provided evidence that some newer antihyperglycemic agents can significantly improve cardiovascular outcomes in the T2DM patient. These clinical studies provide encouraging evidence that certain types of glycemic control may be an important approach to lessening the severity of cardiovascular disease in the T2DM patient.

Management of heart disease in diabetic patients is complex but should follow the same general principles as for patients without diabetes, which includes controlling ischemic symptoms and reducing ischemic burden. The article by Romualdo Belardinelli nicely describes the indications for medical therapy versus coronary revascularization in diabetic patients with both diabetes and ischemic heart disease. Man-

agement issues are also evident in diabetic patients presenting with heart failure. Patients with diabetes are at high risk for developing left ventricular dysfunction and heart failure. The article by Dominic Leung and Melissa Leung describes the need for early comprehensive assessment of cardiac structure and function in diabetics at risk for developing heart disease and the role exercise echocardiography has in this process. Maria Scali also provides an insightful case report as to the need for risk stratification in treating the diabetic with chest pain. A low-cost approach using echocardiography, electrocardiogram changes, and coronary flow reserve provides a versatile approach to treating the diabetic with chest pain. The article by Joao Eduardo Salles provides insights into what the cardiologist needs to know with regard to the new drugs that are now available to control blood glucose in the diabetic, as well as their implications for cardiovascular disease risk.

Diabetes results in some dramatic alterations in energy metabolism in the heart. Diabetes can result in unique changes in cardiac function and metabolism, especially at the level of cardiac energy metabolism. The article by Kim Ho and John Ussher provides an update on what is known about the dramatic switch in energy metabolism from glucose to fatty acid metabolism and the implications of this on cardiac function in the diabetic. These cardiac metabolic changes seen in the diabetic provide an opportunity to treat

heart disease in the diabetic using approaches that directly target cardiac energy metabolism. The article by Gabriele Fragasso and colleagues describes how using the metabolic modulator trimetazidine could be one such approach. Inhibition of fatty acid oxidation has emerged as a new approach to treating ischemic heart disease and heart failure. This type of approach may be particularly relevant in the diabetic with heart disease due to the metabolic switch in the heart toward an excessive use of fatty acids.

Cardiovascular disease has now become the number one cause of death worldwide. The rapid global rise in the incidence of T2DM is an important contributor to this grim statistic. Hopefully, this issue of *Heart and Metabolism* will provide some unique perspectives not only on how the diabetic patient with heart disease should be treated, but also for future direction in how the diabetic patient should be managed. ■

## REFERENCES

1. World Health Organization. Global Report on Diabetes, 2016. Available at: <http://www.who.int/diabetes/global-report/en/>. Published 2016. Accessed December 4, 2016.
2. Seshasai SR, Kaptoge S, Thompson A, et al. Diabetes mellitus, fasting glucose, and risk of cause-specific death. Emerging Risk Factors Collaboration. *N Engl J Med*. 2011;364:829-841.
3. Erqou S, Lee CT, Suffoletto M, et al. Association between glycated haemoglobin and the risk of congestive heart failure in diabetes mellitus: systematic review and meta-analysis. *Eur J Heart Fail*. 2013;15(2):185-193.