Editorial: diabetes and heart failure: pathogenesis and novel therapeutic approac...

Health & Medicine

Editorial on the Research Topic

Diabetes and Heart Failure: Pathogenesis and Novel Therapeutic Approaches

Type 2 diabetes mellitus (T2DM) and Heart Failure (HF) are two complex multifactorial diseases that can coexist and strongly amplify each other, suggesting overlapping mechanisms contributing to disease state. T2DM patients with HF have a higher risk of mortality and hospitalization for HF than HF patients without T2DM. Therefore, there is an increasing necessity to find new diagnostic instruments and treatments to improve clinical outcomes in T2DM subjects with HF (Maack et al., 2018). Several complex pathological mechanisms such as altered cardiac ionic homeostasis, oxidative stress, hyperglycemia-induced cellular damage, and mitochondrial dysfunction are implicated. Importantly, altered cardiac ionic homeostasis is an established signature and driver of HF pathology (Pogwizd et al., 2003), but has been largely neglected in T2DM pathology. Insulin resistance and disturbances in glucose and fatty acid metabolism are currently viewed as major instigators of T2DM (Jia et al., 2018). However, older and recent researches indicate that cardiac ionic disturbances may actually provide an important common ground for both diseases and explain, at least in part, why they mutually amplify each other. Intriguingly, these changes may lead to electrical and mechanical alterations in systolic and diastolic electrical phases. Therefore, in this Research Topic we have tried to bring the two major diseases together by creating a collection of articles written by authors that have focused on common molecular pathways and mechanisms, electrical/mechanical alterations, and subsequently on clinical outcomes in both T2DM and HF.

In the first review by Borghetti et al. emphasis is placed on focusing of diabetic therapies beyond glucose control. Although anti-hyperglycemic drugs are crucial in the management of diabetes by effectively reducing microvascular complications, preventing renal failure, retinopathy, and nerve damage, they have little effect on diabetic cardiomyopathy. Interestingly, several novel drugs have now shown cardiovascular beneficial effects beyond their ability to control glycemia, such as GLP-1 receptor agonists and sodium-glucose co-transporter 2 inhibitors. In addition, the recent development of modulating the expression of specific cardiac genes or non-coding RNAs *in vivo* for therapeutic purpose, has opened up the possibility to regulate the expression of key players in the development/progression of diabetic cardiomyopathy.

The review by Bajpai and Tilley discusses the roles of leukocytes and particularly neutrophils, macrophages, and lymphocytes in the appearance of myocardial infarction and heart failure during diabetes. Cardiac injury in diabetes, a chronic inflammatory disease, is linked to increased leukocyte mobilization and the expression of pro-inflammatory cytokines and appearance of oxidative stress. The lessons learned from experimental diabetes models in rodents, including the popular streptozotocin-induced Type I diabetes rodent model, are implemented to human patients, and the authors conclude that further studies are necessary to fully apprehend the potential alterations in leukocyte phenotypes and the molecular mechanisms responsible for diabetes.

The review by Grisanti highlights the impact of diabetes on the electrical conduction system in the heart, resulting in atrial fibrillation and ventricular arrhythmias, with a focus on molecular mechanisms, cardiac alterations and therapeutic ameliorations, with a particular emphasis on the contribution of oxidative stress to the pathogenesis of cardiac arrhythmias. The author states that modifications induced by diabetes within the heart change the electrical signaling and conduction in turn altering ion channels and gap junctions' expression and function. Still, antiarrhythmic drugs are effective in the course of diabetes but their mode of action remains to be better characterized.

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Pogwizd, S. M., Sipido, K. R., Verdonck, F., and Bers, D. M. (2003). Intracellular Na in animal models of hypertrophy and heart failure: contractile function and arrhythmogenesis. *Cardiovasc. Res.* 57, 887–896. doi: 10. 1016/S0008-6363(02)00735-6