Editorial

The Different Facets of Cardio-metabolic Diseases and Related Complications: Current Perspective and Future Developments

Cardio-metabolic complications are multifactorial diseases with different facets, many of which are poorly understood, although genetics, epigenetics, humoral, habitual and environmental factors may be involved. Moreover, with the dramatic escalation of obesity, diabetes and hypertension in all segments of the population including adults, adolescence and children, the incidence of cardio-metabolic disease and related complications will further increase. Therefore, this special issue puts together a collection of review articles by leading experts in the area to give a critical appraisal of the current state of knowledge and recent accomplishments as well as challenges and future directions.

The role of pigment epithelium-derived factor (PEDF) in cardiometabolic disease is among the emerging themes of scientific interest, with the role of pigment epithelium-derived factor (PEDF) in cardiometabolic disease. PEDF is a glycoprotein that has been shown to possess anti-thrombotic and anti-fibrotic properties besides its effects against oxidative stress and inflammatory. Accordingly, in an article featuring in this special issue, Yamagishi & Matsui underscored the role of PEDF in cardiometabolic diseases and related complications, with particular focus on diseases such as diabetic retinopathy, renal dysfunction, hepatic insufficiency and disorders affecting the male and female reproductive systems. The authors discussed the potential clinical relevance of modulating PEDF for the prevention and management of these cardiometabolic disorders. In another related article, Shinlapawittayatorn et al. gave profound insights on the effects of obese insulin-resistance, a common risk factor for ischemic heart disease on ischemia-reperfusion injury of the heart. Amongst the pertinent points raised by the authors is whether improving insulin sensitivity by pharmacological interventions could ameliorate reperfusion induced myocardial injury. Dysfunctional myocardium is a common complication of diabetes. To expatiate on this problem further, Tarquini et al. wrote an article about diabetic cardiomyopathy, a pathophysiological condition in which the myocardial interstitium undergoes alterations resulting in abnormal contractile function. The authors reported that in the early stages of the disease, diastolic dysfunction is the only abnormality, but systolic dysfunction supervenes at later stages with impaired left ventricular ejection fraction. Furthermore, the authors underscored a putative correlation between diabetes and cardiomyopathy, especially in diabetic patients with co-morbid with microvascular complications, and suggested that this correlation parallels the duration and severity of hyperglycemia.

Besides the heart, the kidney is an important organ for the regulation of extracellular volume and thus blood pressure. Renal dysfunction is associated with hypertension, proteinuria and kidney failure. Accordingly, novel insights on structures of the kidney, such as the glomerular filtration barrier, are important. In a related article that appears in this special issue, Ndisang wrote about the putative cross-talk amongst the major components of the glomerular filtration barrier including podocytes, endothelial cells and the basement membrane, and how the dynamic interplay and interaction between these constituents may be fundamental for effective filtration. Furthermore, the author highlighted some of the challenging issues about the interaction between: (i) glomerular endothelial cells and podocytes; (ii) glomerular endothelial cells and glomerular basement membrane; (iii) podocytes and glomerular basement membrane; (iv) the simultaneous interaction among the three components, and suggested that the elucidation of these multifaceted interactions will pave the way for greater understanding of the pathophysiology of kidney dysfunction and the formulation of novel therapies for kidney disease. In another related article, Krämer and Weidemann gave their insights on Fabry disease, pathophysiological condition associated with X-linked lysosomal storage caused by deficient activity of α-galactosidase A and intracellular accumulation of globotriaosylceramide in different physiological entities such as the vascular endothelium, nervous system, eyes, skin, heart and kidneys.

A wide variety of drugs are used for the treatment and management of cardiometabolic diseases. For example, proprotein convertase subtilisin/kexin 9 (PCSK9) inhibitors are used to lower low-density lipoprotein cholesterol in patients with dyslipidemia, hypercholesterolemia or atherosclerosis. In an article, in this special issue, Schremla and
Gouni-Berthold gave an in-depth insight on the use of monoclonal antibodies against PCSK9 to attenuate hypercholesterolemia, and reported that antibody-derived PCSK9 drugs such as alirocumab (Praluent®) and evolocumab (Repatha®) can reduce low-density lipoprotein cholesterol by 70%. Generally, drugs are routinely reviewed for their efficacy and safety. In this light, Eleftheriadou and co-workers insights on the cardiovascular safety of older and newer anti-diabetic medications. The authors reported that metformin, a first line drug for the treatment of type 2 diabetes, is also endowed with cardio-protective effects and should be considered the primary choice, while second line agents such as empagliflozin, liraglutide and semaglutide are reasonable options for patients with cardiovascular disease, whereas the class of sulfonylureas with the exception of gliclazide should be administered to diabetic patients co-morbid with other cardiometabolic diseases. In addition, the authors reported that Saxagliptin, alogliptin, sitagliptin and lixisenatide have been evaluated in cardiovascular safety trials and were shown to have neutral effects on cardiovascular outcomes, whereas pioglitazone has some cardiovascular benefits. However, Saxagliptin and alogliptin should be avoided in patients with heart failure. Consistently, in another article featuring in this special issue, Schmitz and Gouni-Berthold gave clinical evidence on the efficacy and safety of volanesorsen for the treatment of hypertriglyceridemia.

Besides, drugs and other pharmaceutical formulations, dietary fibres and polyphenols are cyto-protective. Accordingly, the protective effects of dietary fibres and the antioxidant and anti-inflammatory properties of polyphenols such as curcumin, quercetin, genistein, caffeic acid phenethyl ester were examined by Pittala and co-workers. They discussed the effects of various naturally occurring polyphenols in the management of metabolic dysfunctions

Collectively, the contributions of the authors of this special issue have underscored to the complexity of cardiometabolic diseases, highlighting the different facets, the accomplishments to date, the challenges that obscure the horizon and the prospects for the future, to which we can all look toward with some degree of optimism.

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