Editorial

Diabetic cardiomyopathy due to metabolic maladaptation

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The current scenario of diabetic population is assuming an alarming proportion, 463 million (Age group 20-79 years) are affected. This staggering number is expected to 700 million by 2045 (International Diabetes Federation, 2020). Diabetes and consequent heart ailments are proven. Framingham Heart Study identified Diabetes (T2DM) as an independent risk factor for both cardiovascular morbidity and mortality in T2DM patients, out of which a significant population suffer from Diabetic Cardiomyopathy a distinct clinical entity. The incidence of cardiac events is significantly enhanced in T2DM population; also, the recovery rate from such events is significantly lower in Diabetics. Among various factors contributing to pathophysiological alterations to cardiac dysfunctions result from maladaptive changes in myocardial metabolism. Marked alterations occur in cardiac metabolism in terms of availability of substrates and their subsequent metabolism in an altered milieu of flawed insulin signalling, reduced glucose uptake inside the cell, deranged mitochondrial function and altered gene regulation in diabetic patients. The derangement is reflected in changes of substrate utilization in diabetic hearts where fatty acid oxidation is enhanced with concomitant diminishing utilization of glucose resulting increase in myocardial oxygen consumption with attendant reduced efficiency in heart function.[1]

Altered cardiac metabolism

Why does this metabolic maladaptation in myocardium take place? There are many changes occur in micro and macro environment in the global scheme of metabolism is changed in the substrate influx in myocardium when free fatty acid availability is increased. Another significant alterations diabetic heart remains aberrant insulin signaling in myocardium leading to decreased glucose transporter (GLUT) mediated uptake.[2] Altered substrate influx with concomitant utilization of free fatty acid during stress and ischaemia makes diabetic heart more vulnerable to ischemic insult and other challenges. Thus altered metabolic status in diabetic heart makes it less adaptable to ischemia and cardiac events than non diabetic individuals. Given the metabolic alterations of the diabetic heart at rest and during episodes myocardial ischaemia, a therapeutic approach aimed at an improvement of cardiac metabolism through manipulations of the utilization of metabolic substrates should result in an improvement of myocardial ischaemia and of left ventricular function. Partial fatty acid oxidation in heart like Trimetazidine proves to be beneficial in clinical setting. Modulation of myocardial free fatty acid oxidation results reduced myocardial oxygen consumption resulting in a more happy and efficient heart. The metabolic modulation of altered myocardial metabolism in heart often renders to be helpful in T2DM patients and non diabetic cardiac patients, more so in the former cohorts.

Mitochondrial dysfunction: Can spring be far behind?

No prize for guessing. Altered myocardial energetics and mitochondrial dysfunction results will obviously pose a chicken – egg paradox in T2DM patients as to whether myocardial dysfunction results due to altered milieu or adversely affected mitochondrial function leads to maladaptive cardiac metabolic changes. Impaired myocardial insulin signaling promotes oxidative stress and mitochondrial uncoupling, which, together with reduced tricarboxylic acid and fatty acid oxidative capacity, impairs mitochondrial energetics. This study identifies specific contributions of impaired insulin action to mitochondrial dysfunction in the heart. Altered mitochondrial gene expression has been reported in T2 DM and various non–diabetic cardiomyopathies.[3]

Genomics and altered cardiac metabolism

The recent advances in genomics provides insights into genome structure, genomic stability, gene expression and metabolomics, proteomics provide insights into cardiac metabolism in clinical settings that compromise cardiac functions. Genome-wide association studies (GWASs) provide an unprecedented opportunity to examine, on a large scale, the association of common genetic variants with complex diseases like T2 DM, Metabolic syndrome and cardiovascular diseases. Identifying the genomic association leads to further study of functional genomics to study functions of the genes and their products. Transcriptome analysis may lead to development of therapeutic targets that may address pathogenicity of T2DM and Cardiomyopathy together.[4]

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Conflicts of interest

Author declares that there is no conflict of interest.

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