

Commentary to the article

“Metabolic syndrome is associated with different clinical outcome after cardiac resynchronization therapy in patients with ischemic and non-ischemic cardiomyopathy”

I have read the article entitled “Metabolic syndrome is associated with different clinical outcome after cardiac resynchronization therapy in patients with ischemic and non-ischemic cardiomyopathy” by Szepietowska et al. [1], recently published in “Cardiology Journal”, with great interest. The investigators reported that obese non-ischemic cardiomyopathy patients derive significant benefit from cardiac resynchronization with defibrillator therapy (CRT-D) if they present with metabolic syndrome (MS), whereas obese patients without MS show no significant reduction in events. On the contrary, obese ischemic cardiomyopathy patients with MS show no benefit from cardiac resynchronization therapy (CRT), while obese ischemic patients without MS show significant reduction in the risk of events [1]. Szepietowska et al. [1] have claimed that intrinsic properties of myocardium fuel metabolism affected by MS may play a role in response to CRT.

Because of continuous contractile activity, the heart has a very high energy demand. About 95% of this energy is normally obtained by production of adenosine triphosphate (ATP) from mitochondrial oxidative metabolism, while the remaining 5% originates from glycolytic ATP production. The source of fuel for mitochondrial oxidative metabolism normally comes from a balance between fatty acids and carbohydrates, and to a lesser degree ketones and amino acids [2].

In the event of heart failure, there is a switch from mitochondrial oxidative metabolism to an increase in glucose uptake and glycolysis [3]. This increase in glucose uptake and glycolysis can occur even though mitochondrial glucose oxidation is impaired, resulting in an uncoupling of glycolysis from glucose oxidation. This uncoupling produces lactate and $[H^+]$, which decreases the efficiency of the heart [3]. The heart has a strict reciprocal relationship between fatty acid oxidation and glucose oxidation, so that an increase in fatty acid oxidation is associated with decrease in glucose oxidation and vice versa [2].

Trimetazidine is a fractional fatty acid oxidation inhibitor that inhibits 3-ketoacyl CoA thiolase, one of the enzymes of fatty acid beta-oxidation. This results in an increase in glucose oxidation. Trimetazidine improves endothelial function, reduces calcium overload and free radical-induced injury, as well as inhibits cell apoptosis and cardiac fibrosis via increased high-energy phosphate levels [4].

Brottier et al. [5] demonstrated that trimetazidine therapy was related to improvement in left ventricular function. El-Kady et al. [6] reported that trimetazidine could reduce the risk of cardiovascular events in heart failure patients.

In the light of this knowledge, trimetazidine therapy could influence response to CRT treatment in patients with heart failure. Authors should elucidate the relationship between trimetazidine treatment and response to CRT treatment.

Conflict of interest: None declared

References

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Levent Cerit, Assistant Professor
 Department of Cardiology, Near East University, Cyprus,
 e-mail: drcerit@hotmail.com