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# Letters to the Editor

## Could Branched-Chain Amino Acids Be a New Landmark in Metabolic Syndrome and Cardiac Arrhythmias?

### To the Editor:

We read with great interest the article published in the *Canadian Journal of Cardiology*, entitled "Sudden Cardiac Death in Diabetes and Obesity: Mechanisms and Therapeutic Strategies by Remme."[1] We would like to provide some comments on the issue and article.

Branched-chain amino acids (BCAAs) are essential amino acids; a deficiency in BCAAs leads to downregulation of signalling through the mammalian target of rapamycin (mTOR), which is a central regulator of cellular metabolism. It is assumed that persistent activation of the mTOR signalling pathway by increased BCAA concentrations plays a role in the pathogenesis of insulin resistance via interference with insulin signalling and increased degradation of insulin receptor substrates. Some studies have demonstrated that 1,25-Dihydroxyvitamin D (1,25-[OH]2D) augments BCAA catabolism, which leads to the downregulation of mTOR activation and improvement in insulin resistance.[2]

Conversely, different studies that focused on melatonin reported that angiotensin-II-induced atrial BCAA accumulation aggravates tissue fibrosis and mitochondrial reactive oxygen species damage in mice, which is possibly linked to atrial fibrillation (AF). Melatonin prevented development of AF by increasing BCAA catabolism and attenuating atrial remodelling by activating the PKG-CREB-KLF15 axis.[3]

Regarding the relationship between BCAAs and obesity and diabetes, BCAAs have been involved in platelet activity. The elevated levels of BCAAs and their catabolites in platelets may be responsible for the high platelet activity in type 2 diabetes mellitus.[4] Tropomodulin-3 propionylation by catabolites of BCAA increases platelet activity and consequently increases the risk of arterial thrombosis. In this study, BCAAs were also shown to significantly promote the aggregation and degranulation of human platelets.[4] This can be considered to be another mechanism in which BCAAs can trigger processes associated with myocardial ischemia with the changes in cardiac microstructure and increased proarrhythmic effects and sudden cardiac death.

In considering the results of these studies, we believe that although the number of human studies remains insufficient, as many cellular reactions that are directly or indirectly related to BCAAs are clarified, their effects on clinical practice will be confirmed.

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### Disclosures

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